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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Dec 17   The CA Lexicon available in the CAPLUS and CA files
 NEWS  3  Feb 06   Engineering Information Encompass files have new names
 NEWS  4  Feb 16   TOXLINE no longer being updated
 NEWS  5  Apr 23   Search Derwent WPINDEX by chemical structure
 NEWS  6  Apr 23   PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
 NEWS  7  May 07   DGENE Reload
 NEWS  8  Jun 20   Published patent applications (A1) are now in USPATFULL
 NEWS  9  JUL 13   New SDI alert frequency now available in Derwent's
                   DWPI and DPCI
 NEWS 10  Aug 23   In-process records and more frequent updates now in
                   MEDLINE
 NEWS 11  Aug 23   PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
 NEWS 12  Aug 23   Adis Newsletters (ADISNEWS) now available on STN

 NEWS EXPRESS  August 15 CURRENT WINDOWS VERSION IS V6.0c,
               CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP),
               AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
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=> file registry

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STRUCTURE FILE UPDATES: 29 AUG 2001 HIGHEST RN 353726-54-2
DICTIONARY FILE UPDATES: 29 AUG 2001 HIGHEST RN 353726-54-2

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

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Structure search limits have been increased. See HELP SLIMIT for details.

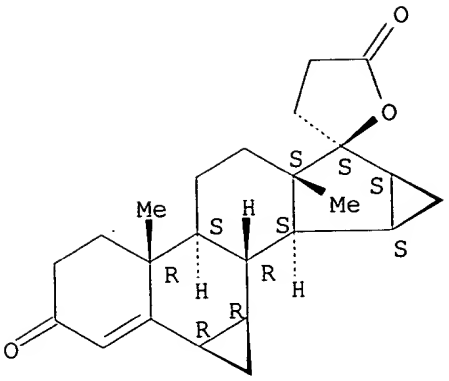
=> s drospirenone/cn

L1 1 DROSPIRENONE/CN

=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 67392-87-4 REGISTRY
CN Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl-, (2'S,6R,7R,8R,9S,10R,13S,14S,15S,16S)-(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl-,
[6R-(6.alpha.,7.alpha.,8.beta.,9.alpha.,10.beta.,13.beta.,14.alpha.,15.alpha.,16.alpha.,17.beta.)]-
OTHER NAMES:
CN 1,2-Dihydrospirorenone
CN 3-Oxo-6.beta.,7.beta.:15.beta.,16.beta.-dimethylene-17.alpha.-pregn-4-en-21,17-carbolactone
CN Dihydrospirorenone
CN **Drospirenone**
CN ZK 30595
FS STEREOSEARCH
MF C24 H30 O3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMLIST, CIN, DDFU, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



70 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
70 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s ethinylestradiol/cn

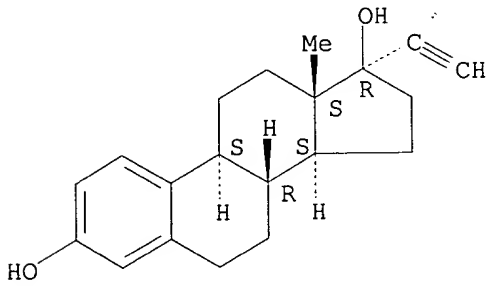
L2 1 ETHINYLESTRADIOL/CN

=> d

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 57-63-6 REGISTRY
CN 19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 19-Nor-17.alpha.-pregna-1,3,5(10)-trien-20-yne-3,17-diol (6CI, 7CI, 8CI)
OTHER NAMES:
CN 17-Ethinyl-3,17-estradiol
CN 17-Ethinylestradiol
CN 17-Ethynyl-3,17-dihydroxy-1,3,5-oestratriene
CN 17-Ethynylestra-1,3,5(10)-triene-3,17.beta.-diol
CN 17-Ethynylestradiol
CN 17-Nor-17.alpha.-pregna-1,3,5-(10)-trien-20-yne-3,17-diol
CN 17.alpha.-Ethinyl-1,3,5(10)-estratriene-3,17-diol
CN 17.alpha.-Ethinyl-17.beta.-estradiol
CN 17.alpha.-Ethinyl-3,17-dihydroxy-.DELTA.1,3,5-estratriene
CN 17.alpha.-Ethinylestra-1,3,5(10)-triene-3,17.beta.-diol
CN 17.alpha.-Ethinylestradiol
CN 17.alpha.-Ethynylestra-1,3,5(10)-triene-3,17.beta.-diol
CN 17.alpha.-Ethynylestradiol
CN 19-Nor-17.alpha.-pregna-1,3,5(10)-trien-20-yne-3,17.beta.-diol
CN Amenoron
CN Chee-O-Gen
CN Chee-O-Genf
CN Diogyn E
CN Dyloform
CN Esteed
CN Estigyn
CN Estinyl
CN Eston-E
CN Estoral
CN Estorals
CN Estradiol, 17-ethynyl-
CN Ethidol
CN Ethinoral
CN **Ethinylestradiol**
CN Ethinyloestradiol
CN Ethynylestradiol

CN Ethynyloestradiol
CN Eticyclin
CN Eticyclol
CN Etinestrol
CN Etinestryl
CN Etinoestryl
CN Etistradiol
CN Follicoral
CN Ginestrene
CN Inestra
CN Linoral
CN Lynoral
CN Menolyn
CN Microfollin
CN neo-Estrone
CN Novestrol
CN Oradiol
CN Orestralyn
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS STEREOSEARCH
DR 77538-56-8
MF C20 H24 O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, ULIDAT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



3372 REFERENCES IN FILE CA (1967 TO DATE)
66 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3377 REFERENCES IN FILE CAPLUS (1967 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> file embase biosis medline caplus uspatfull

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=> s drospirenone or 67392-87-4/rn

'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L3 175 DROSPIRENONE OR 67392-87-4/RN

=> s ethinylestradiol or 57-63-6/rn

'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L4 16773 ETHINYLESTRADIOL OR 57-63-6/RN

=> s l3 and l4

L5 90 L3 AND L4

=> s contracepti?

L6 117905 CONTRACEPTI?

=> s l5 and l6

L7 77 L5 AND L6

=> dup rem l7

PROCESSING COMPLETED FOR L7
L8 51 DUP REM L7 (26 DUPLICATES REMOVED)

=> s l8 and py<1999

2 FILES SEARCHED...
4 FILES SEARCHED...
L9 23 L8 AND PY<1999

=> d l9 1-23 ab bib kwic

L9 ANSWER 1 OF 23 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AB Endogenous 17.beta.-estradiol (E2) and low parenteral doses of exogenous E2 are vasodilators. High dose estrogens, especially **ethinylestradiol** (EE) and mestranol, stimulate the synthesis of hepatic proteins including coagulation factors, sex hormone binding globulin, and angiotensinogen (Aogen). In the steady state, high plasma levels of Aogen produce only a very small increase of angiotensin II (AII) and plasma renin activity, because AII inhibits the secretion of renin and lowers plasma renin concentration. However, the increase in AII is sufficient for a slight reduction in renal blood flow and a slight increase in exchangeable sodium and blood pressure; in susceptible women,

blood pressure may rise considerably. Effects of estrogens on the brain may also be involved in blood pressure changes. Endogenous progesterone is a mineralocorticoid receptor antagonist. Endogenous or exogenous progesterone leads to sodium loss and a compensatory increase in renin secretion, plasma renin activity, AII, and plasma aldosterone, e.g. in the second half of the menstrual cycle. Synthetic progestogens are commonly devoid of the mineralocorticoid receptor antagonistic effect of progesterone, and some are weak estrogen receptor agonists. Combined use of EE and synthetic progestogens may therefore enhance estrogen effects on body sodium and blood pressure. A new progestogen (**Drospirenone**) with an antimineralocorticoid effect like that of progesterone is described that slightly lowers body weight and blood pressure in a **contraceptive** formulation together with EE. An almost ideal oral **contraceptive** would be a progestogen like **Drospirenone** together with a low dose natural estrogen that does not stimulate Aogen synthesis. Since most oral formulations for postmenopausal estrogen replacement also stimulate hepatic protein synthesis (including Aogen) to some extent, the transdermal route of E2 application for **contraceptive** purposes should also be investigated, since it has a reduced potential for undesirable side effects.

AN 96145321 EMBASE
DN 1996145321
TI Effects of estrogens and progestogens on the renin-aldosterone system and blood pressure.
AU Oelkers W.K.H.
CS Division of Endocrinology, Klinikum Benjamin Franklin, Hindenburgdamm 30,12200 Berlin, Germany
SO Steroids, (1996) 61/4 (166-171).
ISSN: 0039-128X CODEN: STEDAM
CY United States
DT Journal; Conference Article
FS 003 Endocrinology
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
SO Steroids, (1996) 61/4 (166-171).
ISSN: 0039-128X CODEN: STEDAM
AB Endogenous 17.beta.-estradiol (E2) and low parenteral doses of exogenous E2 are vasodilators. High dose estrogens, especially **ethinylestradiol** (EE) and mestranol, stimulate the synthesis of hepatic proteins including coagulation factors, sex hormone binding globulin, and angiotensinogen (Aogen). In. . . use of EE and synthetic progestogens may therefore enhance estrogen effects on body sodium and blood pressure. A new progestogen (**Drospirenone**) with an antimineralocorticoid effect like that of progesterone is described that slightly lowers body weight and blood pressure in a **contraceptive** formulation together with EE. An almost ideal oral **contraceptive** would be a progestogen like **Drospirenone** together with a low dose natural estrogen that does not stimulate Aogen synthesis. Since most oral formulations for postmenopausal estrogen replacement also stimulate hepatic protein synthesis (including Aogen) to some extent, the transdermal route of E2 application for **contraceptive** purposes should also be investigated, since it has a reduced potential for undesirable side effects.
CT Medical Descriptors:
*blood pressure
*renin angiotensin aldosterone system
aldosterone blood level
body weight
conference paper
contraception

estrogen therapy
female
hormone action
human
kidney blood flow
oral drug administration
plasma renin activity
renin release
sodium urine level
*angiotensinogen: EC, endogenous compound
*estradiol: EC, endogenous compound
***ethinylestradiol: EC, endogenous compound**
*mestranol: EC, endogenous compound
angiotensin: EC, endogenous compound
drospirenone
estrogen: EC, endogenous compound
ethinylestradiol plus levonorgestrel
gestagen
progesterone
unclassified drug

RN (angiotensinogen) 11002-13-4, 64315-16-8; (estradiol) 50-28-2; (**ethinylestradiol**) 57-63-6; (mestranol) 72-33-3; (angiotensin) 11128-99-7, 1407-47-2; (**ethinylestradiol** plus levonorgestrel) 39366-37-5; (progesterone) 57-83-0

L9 ANSWER 2 OF 23 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AB Combined hormonal oral **contraceptives** (OCs) may lead to a mild rise in blood pressure and body weight. In rare instances, large increments in blood pressure are measured. We investigated the effect of a combination of ethinyl estradiol (EE) plus a progestogen with antimineralocorticoid, i.e. natriuretic, properties [**Drospirenone** (DRSP)] on body weight, blood pressure, the renin-aldosterone system, atrial natriuretic factor, plasma lipids, and glucose tolerance. It is anticipated that this will lead to the development of an OC that does not raise body weight or blood pressure. Four groups of 20 women each received 30 .mu.g EE plus 3 mg DRSP (group A), 20 .mu.g EE plus 3 mg DRSP (group B), 15 .mu.g EE plus 3 mg DRSP (group C), and, as a control OC, 30 .mu.g EE plus 150 .mu.g levonorgestrel (Microgynon, Schering; group D) for 6 months. During the OC-free control cycles before and after treatment and throughout treatment, the target parameters were measured. Between the pretreatment cycle and the sixth treatment cycle, mean body weight fell by 0.8 to 1.7 kg in groups A, B, and C ($P < 0.05$ vs. D), whereas it rose by 0.7 kg in group D. Systolic and diastolic blood pressures fell by 1-4 mm Hg in groups A, B, and C (significant for A and C vs. D) and increased by 1-2 mm Hg in group D. Renin substrate rose equally in all groups ($P < 0.05$), whereas PRA and plasma aldosterone rose significantly only in the DRSP groups, presumably due to sodium loss. In the DRSP groups, high density lipoprotein cholesterol rose ($P < 0.05$), in contrast to group D. Low density lipoprotein cholesterol fell slightly ($P > 0.05$), whereas triglyceride levels showed a stronger increase in the DRSP groups ($P < 0.05$) than in group D. All groups attained good cycle control; group A had the best. Side-effects were minimal. To our knowledge, this is the first report on a combined OC that leads to a small decrease in body weight and blood pressure. It may be especially beneficial for women susceptible for a gain in weight and a rise in blood pressure.

AN 95181789 EMBASE

DN 1995181789

TI Effects of a new oral **contraceptive** containing an antimineralocorticoid progestogen, **drospirenone**, on the renin-aldosterone system, body weight, blood pressure, glucose tolerance, and lipid metabolism.

AU Oelkers W.; Foidart J.M.; Dombrovicz N.; Welter A.; Heithecker R.

CS Klinikum Steglitz der FUB, Abt. Freien Univ. Berlin Endokrinol., Hindenburgdamm 30,12200 Berlin, Germany
SO Journal of Clinical Endocrinology and Metabolism, (1995) 80/6 (1816-1821).
ISSN: 0021-972X CODEN: JCEMAZ
CY United States
DT Journal; Article
FS 003 Endocrinology
010 Obstetrics and Gynecology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
TI Effects of a new oral **contraceptive** containing an antimineralocorticoid progestogen, **drospirenone**, on the renin-aldosterone system, body weight, blood pressure, glucose tolerance, and lipid metabolism.
SO Journal of Clinical Endocrinology and Metabolism, (1995) 80/6 (1816-1821).
ISSN: 0021-972X CODEN: JCEMAZ
AB Combined hormonal oral **contraceptives** (OCs) may lead to a mild rise in blood pressure and body weight. In rare instances, large increments in blood. . . measured. We investigated the effect of a combination of ethinyl estradiol (EE) plus a progestogen with antimineralocorticoid, i.e. natriuretic, properties [**Drospirenone** (DRSP)] on body weight, blood pressure, the renin-aldosterone system, atrial natriuretic factor, plasma lipids, and glucose tolerance. It is anticipated. . .
CT Medical Descriptors:
*hypotension
*renin . . . side effect
human
human experiment
lipid blood level
lipid metabolism
mastalgia: SI, side effect
oral drug administration
plasma renin activity
priority journal
randomized controlled trial
renin substrate
systolic blood pressure
weight reduction
***ethinylestradiol: CT, clinical trial**
***ethinylestradiol: CB, drug combination**
***ethinylestradiol: AE, adverse drug reaction**
*gestagen: CB, drug combination
*gestagen: CT, clinical trial
*gestagen: AE, adverse drug reaction
aldosterone: EC, endogenous compound
drospirenone: AE, adverse drug reaction
drospirenone: CT, clinical trial
drospirenone: CB, drug combination
ethinylestradiol plus levonorgestrel
high density lipoprotein cholesterol: EC, endogenous compound
low density lipoprotein cholesterol: EC, endogenous compound
mineralocorticoid antagonist
oral contraceptive agent: CT, clinical trial
oral contraceptive agent: AE, adverse drug reaction
triacylglycerol: EC, endogenous compound
unclassified drug
RN (**ethinylestradiol**) 57-63-6; (aldosterone) 52-39-1, 6251-69-0; (**ethinylestradiol** plus levonorgestrel) 39366-37-5

L9 ANSWER 3 OF 23 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AB **Drospirenone** (ZK 30595; 6.beta., 7.beta., 15.beta.,

16.beta.-dimethylen-3-oxo-17.alpha.-pregn-4-ene-21, 17-carbo-lactone) is a
novel progestogen under clinical development. Potential applications include oral **contraception**, hormone replacement therapy and treatment of hormonal disorders. **Drospirenone** is characterized by a pharmacodynamic profile very closely related to that of progesterone.

The progestogenic activity of **drospirenone** has been analysed in a variety of animal models. The compound efficiently promotes the maintenance of pregnancy in rats, inhibits ovulation in rats and stimulates endometrial transformation in the rabbit. Furthermore, **drospirenone** shows potent antigonadotropic, i.e, testosterone-lowering, activity in male cynomolgus monkeys. The progestogenic potency of **drospirenone** was found to be in the range of that of norethisterone acetate or cyproterone acetate. Like progesterone, **drospirenone** has been shown to have an antimineralocorticoid effect in rats and humans. It has now been demonstrated that the compound has a longlasting natriuretic activity in rats on administration of a daily dose of 10 mg s.c, for three weeks. Under identical conditions, spironolactone, a widely-used antimineralocorticoid, becomes ineffective after the initial treatment phase. **Drospirenone** exhibits antiandrogenic activity in castrated, testosterone-substituted male rats as shown by dose-dependent inhibition of accessory sex organ growth (prostate, seminal vesicles). In this model, the potency of **drospirenone** was found to. be about one-third that of cyproterone acetate. The compound is devoid of androgenic, estrogenic, glucocorticoid and antiglucocorticoid activity. Possible drug interaction between **drospirenone** and **ethinylestradiol** (EE) was also investigated. EE did not interfere with either the progestogenic or the antimineralocorticoid activity of **drospirenone**. In conclusion, **drospirenone** represents a novel type of synthetic progestogen since it combines potent progestogenic characteristics with antimineralocorticoid and antiandrogenic activity. Thus, the pharmacological profile of **drospirenone** is more closely related to that of the natural hormone progesterone than is that of any other synthetic progestogen in use today. Therefore, **drospirenone** is anticipated to give rise to a number of additional health benefits both for users of oral **contraceptives** and hormone replacement therapy recipients.

AN 95078874 EMBASE
DN 1995078874
TI **Drospirenone**: A novel progestogen with antimineralocorticoid and antiandrogenic activity. Pharmacological characterization in animal models.
AU Muhn P.; Krattenmacher R.; Beier S.; Elger W.; Schillinger E.
CS Schering AG,D-13342 Berlin, Germany
SO Contraception, (1995) 51/2 (99-110).
ISSN: 0010-7824 CODEN: CCPTAY
CY United States
DT Journal; Article
FS 003 Endocrinology
010 Obstetrics and Gynecology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
TI **Drospirenone**: A novel progestogen with antimineralocorticoid and antiandrogenic activity. Pharmacological characterization in animal models.
SO Contraception, (1995) 51/2 (99-110).
ISSN: 0010-7824 CODEN: CCPTAY
AB **Drospirenone** (ZK 30595; 6.beta., 7.beta., 15.beta., 16.beta.-dimethylen-3-oxo-17.alpha.-pregn-4-ene-21, 17-carbo-lactone) is a
novel progestogen under clinical development. Potential applications

include oral **contraception**, hormone replacement therapy and treatment of hormonal disorders. **Drospirenone** is characterized by a pharmacodynamic profile very closely related to that of progesterone.

The progestogenic activity of **drospirenone** has been analysed in a variety of animal models. The compound efficiently promotes the maintenance of pregnancy in rats, inhibits ovulation in rats and stimulates endometrial transformation in the rabbit. Furthermore, **drospirenone** shows potent antigonadotropic, i.e, testosterone-lowering, activity in male cynomolgus monkeys. The progestogenic potency of **drospirenone** was found to be in the range of that of norethisterone acetate or cyproterone acetate. Like progesterone, **drospirenone** has been shown to have an antimineralocorticoid effect in rats and humans. It has now been demonstrated that the compound. . . 10 mg s.c, for three weeks. Under identical conditions, spironolactone, a widely-used antimineralocorticoid, becomes ineffective after the initial treatment phase. **Drospirenone** exhibits antiandrogenic activity in castrated, testosterone-substituted male rats as shown by dose-dependent inhibition of accessory sex organ growth (prostate, seminal vesicles). In this model, the potency of **drospirenone** was found to. be about one-third that of cyproterone acetate. The compound is devoid of androgenic, estrogenic, glucocorticoid and antiglucocorticoid activity. Possible drug interaction between **drospirenone** and **ethinylestradiol** (EE) was also investigated. EE did not interfere with either the progestogenic or the antimineralocorticoid activity of **drospirenone**. In conclusion, **drospirenone** represents a novel type of synthetic progestogen since it combines potent progestogenic characteristics with antimineralocorticoid and antiandrogenic activity. Thus, the pharmacological profile of **drospirenone** is more closely related to that of the natural hormone progesterone than is that of any other synthetic progestogen in use today. Therefore, **drospirenone** is anticipated to give rise to a number of additional health benefits both for users of oral **contraceptives** and hormone replacement therapy recipients.

CT Medical Descriptors:
***contraception**
*hormone substitution
animal experiment
animal model
article
controlled study
drug activity
drug effect
female
male
nonhuman
rabbit
rat
***ethinylestradiol: IT, drug interaction**
*gestagen: PD, pharmacology
1,2 dihydrospirorenone
drospirenone: PD, pharmacology
drospirenone: IT, drug interaction
zk 30595
unclassified drug

RN (**ethinylestradiol**) 57-63-6; (1,2 dihydrospirorenone) 67392-87-4

L9 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB A method of **contraception** is provided which comprises administering to a female of child bearing age a combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a

daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 23-25 days beginning on day 1 of the menstrual cycle, and wherein the same dosage of the progestin and estrogen combination is administered in each of the 23-25 days. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcryst. cellulose, lactose, potassium polacrillin, magnesium stearate, Opadry pink, PEG-1500, was E, and water q.s.

AN 1998:98330 CAPLUS
DN 128:158938
TI Monophasic **contraceptive** method and kit comprising a combination of a progestin and estrogen
IN Gast, Michael Jay
PA American Home Products Corporation, USA
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804269	A1	19980205	WO 1997-US12795	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2261689	AA	19980205	CA 1997-2261689	19970723 <--
	AU 9738887	A1	19980220	AU 1997-38887	19970723 <--
	AU 726091	B2	20001102		
	BR 9710566	A	19990817	BR 1997-10566	19970723
	CN 1226168	A	19990818	CN 1997-196763	19970723
	EP 956024	A1	19991117	EP 1997-936149	19970723
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	JP 2000515890	T2	20001128	JP 1998-508924	19970723
PRAI	US 1996-686790	A	19960726		
	WO 1997-US12795	W	19970723		

TI Monophasic **contraceptive** method and kit comprising a combination of a progestin and estrogen
PI WO 9804269 A1 **19980205**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804269	A1	19980205	WO 1997-US12795	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2261689	AA	19980205	CA 1997-2261689	19970723 <--
	AU 9738887	A1	19980220	AU 1997-38887	19970723 <--
	AU 726091	B2	20001102		
	BR 9710566	A	19990817	BR 1997-10566	19970723
	CN 1226168	A	19990818	CN 1997-196763	19970723
	EP 956024	A1	19991117	EP 1997-936149	19970723
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	JP 2000515890	T2	20001128	JP 1998-508924	19970723

AB A method of **contraception** is provided which comprises

administering to a female of child bearing age a combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 23-25 days beginning on day 1 of the menstrual cycle, and wherein the same dosage of the progestin and estrogen combination is administered in each of the 23-25 days. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcryst. cellulose, lactose, potassium polacrillin,magnesium stearate, Opadry pink, PEG-1500, was E, and water q.s.

ST oral **contraceptive** progestin estrogen; trimegestone ethinyl estradiol oral **contraceptive**

IT **Contraceptives**
(female; monophasic **contraceptive** method and kit comprising combination of progestin and estrogen)

IT Oral **contraceptives**
Ovarian cycle
(monophasic **contraceptive** method and kit comprising combination of progestin and estrogen)

IT Conjugated estrogens
Estrogens
Progestins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monophasic **contraceptive** method and kit comprising combination of progestin and estrogen)

IT 50-28-2, Estradiol, biological studies 53-16-7, Estrone, biological studies 53-16-7D, Estrone, salts **57-63-6**, Ethinyl estradiol 72-33-3, Mestranol 65928-58-7, Dienogest **67392-87-4**, **Drospirenone** 74513-62-5, Trimegestone
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monophasic **contraceptive** method and kit comprising combination of progestin and estrogen)

L9 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 23-25 consecutive days, a first phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 3-8 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and estrogen combination is administered in each of the 3-8 days. A second phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days, beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 4-15 days, and a third phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 4-15 days provided that the daily dosage of the combination administered in the phase is not the same as the daily dosage of the combination administered in the second

phase and that the daily dosage of the combination administered in the second phase is not the same as the daily dosage of the combination administered in the third phase. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcryst. cellulose, lactose, polacrilin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and wax.

AN 1998:98329 CAPLUS
DN 128:158937
TI Progestin/estrogen oral **contraceptives**
IN Gast, Michael Jay
PA American Home Products Corporation, USA
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804268	A1	19980205	WO 1997-US12786	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2261687	AA	19980205	CA 1997-2261687	19970723 <--
	AU 9738076	A1	19980220	AU 1997-38076	19970723 <--
	AU 713016	B2	19991118		
	EP 917466	A1	19990526	EP 1997-935047	19970723
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	BR 9710565	A	19990817	BR 1997-10565	19970723
	CN 1230888	A	19991006	CN 1997-198093	19970723
	JP 2000515888	T2	20001128	JP 1998-508919	19970723
PRAI	US 1996-686786	A	19960726		
	WO 1997-US12786	W	19970723		

TI Progestin/estrogen oral **contraceptives**
PI WO 9804268 A1 **19980205**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804268	A1	19980205	WO 1997-US12786	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2261687	AA	19980205	CA 1997-2261687	19970723 <--
	AU 9738076	A1	19980220	AU 1997-38076	19970723 <--
	AU 713016	B2	19991118		
	EP 917466	A1	19990526	EP 1997-935047	19970723
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	BR 9710565	A	19990817	BR 1997-10565	19970723
	CN 1230888	A	19991006	CN 1997-198093	19970723
	JP 2000515888	T2	20001128	JP 1998-508919	19970723

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 23-25 consecutive days, a first phase combination of a progestin at a daily dosage of 40-500 .mu.g

trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 3-8 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and estrogen combination is administered in each of the 3-8 days. A second phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days, beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 4-15 days, and a third phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 4-15 days provided that the daily dosage of the combination administered in the phase is not the same as the daily dosage of the combination administered in the second phase and that the daily dosage of the combination administered in the second phase is not the same as the daily dosage of the combination administered in the third phase. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcryst. cellulose, lactose, polacrilin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and wax.

ST oral **contraceptive** progestin estrogen; trimegestone ethinyl estradiol oral **contraceptive**

IT Oral **contraceptives**
(progestin/estrogen oral **contraceptives**)

IT Conjugated estrogens
Estrogens
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestin/estrogen oral **contraceptives**)

IT 50-28-2, Estradiol, biological studies 53-16-7, Estrone, biological studies **57-63-6**, Ethinyl estradiol 57-83-0, Progestin, biological studies 72-33-3, Mestranol 65928-58-7, Dienogest **67392-87-4, Drospirenone** 74513-62-5, Trimegestone
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestin/estrogen oral **contraceptives**)

L9 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB This invention provides a method of **contraception** which comprises administering to a female of child-bearing age a combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g **ethinylestradiol** for 23-25 days beginning on day 1 of the menstrual cycle; wherein the same dosage of the progestin and estrogen combination is administered in each of the 23-25 days, followed by the administration of an estrogen at a daily dosage equiv. in estrogenic activity to 5-15 .mu.g **ethinylestradiol** for 3-5 days, such that the no. of days of administration of the progestin and estrogen combination plus the no. of days of administration of estrogen is equal to 28 per menstrual cycle. For example, during the first 23-25 days of the menstrual cycle, a pill contg. trimegestone 125 and **ethinylestradiol** 15 .mu.g is administered and during the last 3-5 days of the menstrual cycle, a pill contg. 15 .mu.g

ethinylestradiol is administered.

AN 1998:98328 CAPLUS
DN 128:158936
TI Progestin/estrogen oral **contraceptives**
IN Gast, Michael Jay
PA American Home Products Corporation, USA
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804267	A1	19980205	WO 1997-US12789	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9738886	A1	19980220	AU 1997-38886	19970723 <--
PRAI	US 1996-687855		19960726		
	WO 1997-US12789		19970723		

TI Progestin/estrogen oral **contraceptives**
PI WO 9804267 A1 **19980205**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804267	A1	19980205	WO 1997-US12789	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9738886	A1	19980220	AU 1997-38886	19970723 <--

AB This invention provides a method of **contraception** which comprises administering to a female of child-bearing age a combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g **ethinylestradiol** for 23-25 days beginning on day 1 of the menstrual cycle; wherein the same dosage of the progestin and estrogen combination is administered in each of the 23-25 days, followed by the administration of an estrogen at a daily dosage equiv. in estrogenic activity to 5-15 .mu.g **ethinylestradiol** for 3-5 days, such that the no. of days of administration of the progestin and estrogen combination plus the no. of days of administration of estrogen is equal to 28 per menstrual cycle. For example, during the first 23-25 days of the menstrual cycle, a pill contg. trimegestone 125 and **ethinylestradiol** 15 .mu.g is administered and during the last 3-5 days of the menstrual cycle, a pill contg. 15 .mu.g **ethinylestradiol** is administered.

ST progestin estrogen oral **contraceptive** pill; trimegestone **ethinylestradiol** combination oral **contraceptive**

IT Oral **contraceptives**
Tablets (drug delivery systems)
(progestin/estrogen oral **contraceptives**)

IT Conjugated estrogens
Estrogens
Progestins

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestin/estrogen oral **contraceptives**)

IT 50-28-2, 17.beta.-Estradiol, biological studies 53-16-7, Estrone, biological studies **57-63-6**, Ethinyl estradiol 72-33-3, Mestranol 65928-58-7, Dienogest **67392-87-4**, **Drospirenone** 74513-62-5, Trimegestone
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestin/estrogen oral **contraceptives**)

L9 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 28 consecutive days, a first phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, and 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 9-13 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and estrogen combination is administered in each of the 9-13 days. A second phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, and 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 11-15 days beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 11-15 days, and an estrogen phase estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 3-5 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the estrogen is administered in each of the 3-5 days, provided that the daily dosage of second phase progestin is greater than the daily dosage of the first phase progestin and that the daily dosage of the second phase estrogen. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcryst. cellulose, lactose, polacrilin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and wax.

AN 1998:98327 CAPLUS
DN 128:158935
TI Progestin/estrogen oral **contraceptives**
IN Gast, Michael Jay
PA American Home Products Corporation, USA
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804266	A1	19980205	WO 1997-US12788	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9739616	A1	19980220	AU 1997-39616	19970723 <--
PRAI	US 1996-688177		19960726		
	WO 1997-US12788		19970723		

TI Progestin/estrogen oral **contraceptives**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804266 A1		**19980205**		

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PI	WO 9804266	A1	19980205	WO 1997-US12788	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9739616	A1	19980220	AU 1997-39616	19970723 <--

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 28 consecutive days, a first phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, and 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 9-13 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and estrogen combination is administered in each of the 9-13 days. A second phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, and 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 11-15 days beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 11-15 days, and an estrogen phase estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 3-5 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the estrogen is administered in each of the 3-5 days, provided that the daily dosage of second phase progestin is greater than the daily dosage of the first phase progestin and that the daily dosage of the second phase estrogen. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcryst. cellulose, lactose, polacrilin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and wax.

ST oral **contraceptive** progestin estrogen; trimegestone ethinyl estradiol oral **contraceptive**

IT Oral **contraceptives**
(progestin/estrogen oral **contraceptives**)

IT Conjugated estrogens
Estrogens
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestin/estrogen oral **contraceptives**)

IT 50-28-2, Estradiol, biological studies 53-16-7, Estrone, biological studies **57-63-6**, Ethinyl estradiol 57-83-0, Progestin, biological studies 72-33-3, Mestranol 65928-58-7, Dienogest **67392-87-4**, **Drospirenone** 74513-62-5, Trimegestone
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestin/estrogen oral **contraceptives**)

L9 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 23-25 consecutive days, a first phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 9-13 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and estrogen combination is administered in each of the 9-13

days, and a second phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 11-15 days beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 11-15 days, provided that the daily dosage of second phase progestin is greater than the daily dosage of the first phase progestin and that the daily dosage of the second phase estrogen is greater than or equal to the daily dosage of the first phase estrogen. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 10 .mu.g, microcryst. cellulose, lactose, polacrilin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and wax.

AN 1998:98326 CAPLUS
DN 128:158934
TI Biphasic **contraceptive** method and kit comprising a combination of a progestin and estrogen
IN Gast, Michael Jay
PA American Home Products Corporation, USA
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804265	A1	19980205	WO 1997-US12787	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2261748	AA	19980205	CA 1997-2261748	19970723 <--
	AU 9740435	A1	19980220	AU 1997-40435	19970723 <--
	EP 921804	A1	19990616	EP 1997-938011	19970723
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	CN 1226167	A	19990818	CN 1997-196684	19970723
	JP 2000515889	T2	20001128	JP 1998-508920	19970723
PRAI	US 1996-690422	A	19960726		
	WO 1997-US12787	W	19970723		

TI Biphasic **contraceptive** method and kit comprising a combination of a progestin and estrogen
PI WO 9804265 A1 **19980205**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804265	A1	19980205	WO 1997-US12787	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2261748	AA	19980205	CA 1997-2261748	19970723 <--
	AU 9740435	A1	19980220	AU 1997-40435	19970723 <--
	EP 921804	A1	19990616	EP 1997-938011	19970723
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				

CN 1226167 A 19990818 CN 1997-196684 19970723
JP 2000515889 T2 20001128 JP 1998-508920 19970723

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 23-25 consecutive days, a first phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 9-13 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and estrogen combination is administered in each of the 9-13 days, and a second phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 11-15 days beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 11-15 days, provided that the daily dosage of second phase progestin is greater than the daily dosage of the first phase progestin and that the daily dosage of the second phase estrogen is greater than or equal to the daily dosage of the first phase estrogen. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 10 .mu.g, microcryst. cellulose, lactose, polacrilin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and wax.

ST progestin estrogen oral **contraceptive**; trimegestone ethinyl estradiol oral **contraceptive**

IT Oral **contraceptives**
(biphasic **contraceptive** method and kit comprising combination of progestin and estrogen)

IT Conjugated estrogens
Estrogens
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biphasic **contraceptive** method and kit comprising combination of progestin and estrogen)

IT 50-28-2, Estradiol, biological studies 53-16-7, Estrone, biological studies **57-63-6**, Ethinyl estradiol 57-83-0, Progestin, biological studies 72-33-3, Mestranol 65928-58-7, Dienogest **67392-87-4, Drospirenone** 74513-62-5, Trimegestone
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biphasic **contraceptive** method and kit comprising combination of progestin and estrogen)

L9 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 23-25 consecutive days: a first phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg .mu.g **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 3-8 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and estrogen combination is administered in each of the 3-8 days; a second phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg .mu.g **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 4-15 days. A

third phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg .mu.g **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 4-15 days; and an estrogen phase estrogen at a daily dosage equiv. in estrogenic activity to 5-20 .mu.g ethinyl estradiol, for 3-5 days beginning on the day immediately following the last day of administration of the third phase combination, wherein the same dosage of the estrogen is administered in each of the 3-5 days, provided that the daily dosage of the combination administered in the first phase is not the same as the daily dosage of the combination administered in the second phase and that the daily dosage of the combination administered in the second phase is not the same as the daily dosage of the combination administered in the third phase. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcrystaline cellulose, lactose, potassium polacrillin, magnesium stearate, Opadry pink, PEG-1500, was E, and water q.s.

AN 1998:98311 CAPLUS
DN 128:158929
TI Oral **contraceptives** containing combination of a progestin and an estrogen
IN Gast, Michael Jay
PA American Home Products Corporation, USA
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804246	A2	19980205	WO 1997-US12785	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9738885	A1	19980220	AU 1997-38885	19970723 <--
PRAI	US 1996-690439		19960726		
	WO 1997-US12785		19970723		

TI Oral **contraceptives** containing combination of a progestin and an estrogen

PI WO 9804246 A2 **19980205**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804246	A2	19980205	WO 1997-US12785	19970723 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9738885	A1	19980220	AU 1997-38885	19970723 <--

AB A method of **contraception** is provided which comprises administering to a female of child bearing age for 23-25 consecutive days:
a first phase combination of a progestin at a daily dosage of 40-500 .mu.g

trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg .mu.g **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 3-8 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and estrogen combination is administered in each of the 3-8 days; a second phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg .mu.g **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 4-15 days. A third phase combination of a progestin at a daily dosage of 40-500 .mu.g trimegestone, 250 .mu.g-4 mg dienogest, or 250 .mu.g-4 mg .mu.g **drospirenone**, and an estrogen at a daily dosage equiv. in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 4-15 days; and an estrogen phase estrogen at a daily dosage equiv. in estrogenic activity to 5-20 .mu.g ethinyl estradiol, for 3-5 days beginning on the day immediately following the last day of administration of the third phase combination, wherein the same dosage of the estrogen is administered in each of the 3-5 days, provided that the daily dosage of the combination administered in the first phase is not the same as the daily dosage of the combination administered in the second phase and that the daily dosage of the combination administered in the second phase is not the same as the daily dosage of the combination administered in the third phase. An oral **contraceptive** compn. contained trimegestone 125, ethinyl estradiol 15 .mu.g, microcrystaline cellulose, lactose, potassium polacrillin, magnesium stearate, Opadry pink, PEG-1500, was E, and water q.s.

ST oral **contraceptive** progestin estrogen; trimegestone ethinyl estradiol oral **contraceptive**

IT **Contraceptives**
(female; oral **contraceptives** contg. combination of progestin and estrogen)

IT Oral **contraceptives**
Ovarian cycle
(oral **contraceptives** contg. combination of progestin and estrogen)

IT Conjugated estrogens
Estrogens
Progestins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **contraceptives** contg. combination of progestin and estrogen)

IT 50-28-2, Estradiol, biological studies 53-16-7, Estrone, biological studies 53-16-7D, Estrone, salts **57-63-6**, Ethinyl estradiol 72-33-3, Mestranol 65928-58-7, Dienogest **67392-87-4**, **Drospirenone** 74513-62-5, Trimegestone
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **contraceptives** contg. combination of progestin and estrogen)

L9 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB A 2-stage combination for hormonal **contraception** comprises 30-84 daily dosage units of a hormone combination administered to women in 2 stages; in stage 1, an estrogen is administered in combination with a gestagen in an amt. at least sufficient to inhibit ovulation, and in stage 2, only the estrogen is administered. Stage 1 lasts 25-77 days, and begins on day 1 of the menstrual cycle; stage 2 lasts 5, 6, or 7 days. A

dosage unit is thus taken on every day of the cycle. The hormones may also be administered continuously in equiv. amts., e.g. via a transdermal patch. This regimen provides highly effective **contraception** at very low estrogen and total hormone doses, complete control of the menstrual cycle, and a low incidence of follicle development, and minimizes breakthrough bleeding, spotting, and cardiovascular side effects.,. Suitable daily dosages in stage 1 are 1.0-6.0 mg 17.beta.-estradiol and 0.05-0.075 mg Gestodene, and in stage 2, 1.0-6.0 mg 17.beta.-estradiol.

AN 1997:105218 CAPLUS
DN 126:122465
TI **Contraceptive** hormonal combination, kit, and method
IN Schmidt-Gollwitzer, Karin; Klemann, Walter
PA Schering A.-G., Germany
SO Ger. Offen., 15 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19525017	A1	19970102	DE 1995-19525017	19950628 <--
	CA 2225724	AA	19970116	CA 1996-2225724	19960627 <--
	WO 9701342	A1	19970116	WO 1996-DE1192	19960627 <--
	W: AU, BR, CA, CN, CZ, FI, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9663528	A1	19970130	AU 1996-63528	19960627 <--
	EP 835114	A1	19980415	EP 1996-922739	19960627 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1189101	A	19980729	CN 1996-195091	19960627 <--
	BR 9609317	A	19990706	BR 1996-9317	19960627
	JP 11508538	T2	19990727	JP 1996-504097	19960627
	ZA 9605547	A	19970127	ZA 1996-5547	19960628 <--
	NO 9706067	A	19980227	NO 1997-6067	19971223 <--
	US 6027749	A	20000222	US 1998-981488	19980603
	AU 726283	B2	20001102	AU 2000-14858	20000201
PRAI	DE 1995-19525017	A	19950628		
	WO 1996-DE1192	W	19960627		

TI **Contraceptive** hormonal combination, kit, and method
PI DE 19525017 A1 **19970102**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19525017	A1	19970102	DE 1995-19525017	19950628 <--
	CA 2225724	AA	19970116	CA 1996-2225724	19960627 <--
	WO 9701342	A1	19970116	WO 1996-DE1192	19960627 <--
	W: AU, BR, CA, CN, CZ, FI, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9663528	A1	19970130	AU 1996-63528	19960627 <--
	EP 835114	A1	19980415	EP 1996-922739	19960627 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1189101	A	19980729	CN 1996-195091	19960627 <--
	BR 9609317	A	19990706	BR 1996-9317	19960627
	JP 11508538	T2	19990727	JP 1996-504097	19960627
	ZA 9605547	A	19970127	ZA 1996-5547	19960628 <--
	NO 9706067	A	19980227	NO 1997-6067	19971223 <--
	US 6027749	A	20000222	US 1998-981488	19980603
	AU 726283	B2	20001102	AU 2000-14858	20000201

AB A 2-stage combination for hormonal **contraception** comprises 30-84 daily dosage units of a hormone combination administered to women in 2

stages; in stage 1, an estrogen is administered in combination with a gestagen in an amt. at least sufficient to inhibit ovulation, and in stage 2, only the estrogen is administered. Stage 1 lasts 25-77 days, and begins on day 1 of the menstrual cycle; stage 2 lasts 5, 6, or 7 days. A dosage unit is thus taken on every day of the cycle. The hormones may also be administered continuously in equiv. amts., e.g. via a transdermal patch. This regimen provides highly effective **contraception** at very low estrogen and total hormone doses, complete control of the menstrual cycle, and a low incidence of follicle development, and minimizes breakthrough bleeding, spotting, and cardiovascular side effects.,. Suitable daily dosages in stage 1 are 1.0-6.0 mg 17.beta.-estradiol and 0.05-0.075 mg Gestodene, and in stage 2, 1.0-6.0 mg 17.beta.-estradiol.

ST estrogen gestagen **contraceptive**; ovarian cycle control estrogen gestagen

IT **Contraceptives**
(**contraceptive** hormonal combination, kit, and method)

IT Estrogens
Progestins
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**contraceptive** hormonal combination, kit, and method)

IT Ovarian cycle
(regulation of; **contraceptive** hormonal combination, kit, and method)

IT 50-28-2, 17.beta.-Estradiol, biological studies **57-63-6,** Ethynylestradiol 68-22-4, Norethisterone 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 979-32-8, 17.beta.-Estradiol valerate 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene **67392-87-4**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**contraceptive** hormonal combination, kit, and method)

L9 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB An oral **contraceptive** system comprises a series of 23-24 daily dosage units contg. an estrogen and an ovulation-inhibiting amt. of a gestagen, to be followed by a series of 4-10 daily dosage units contg. an estrogen alone. The dosages are such as to minimize the estrogen and total hormone contents of each dosage unit while maintaining high **contraceptive** effectiveness and menstrual cycle control with low incidence of follicle development and side effects. Typical daily dosages are 1.0-4.0 mg 17.beta.-estradiol valerate and 0.05-0.075 mg Gestoden.

AN 1995:902894 CAPLUS

DN 123:296590

TI Estrogen-gestagen combination for hormonal **contraception**

IN Lachnit-Fixson, Ursula; Duesterberg, Bernd; Spona, Juergen

PA Schering A.-G., Germany

SO Ger. Offen., 7 pp.
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4411585	A1	19951005	DE 1994-4411585	19940330 <--
	WO 9526730	A1	19951012	WO 1995-EP1190	19950330 <--
	W: AU, BG, BR, CA, CN, CZ, EE, FI, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RO, RU, SI, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9520735	A1	19951023	AU 1995-20735	19950330 <--
	EP 750501	A1	19970102	EP 1995-913171	19950330 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

	HU 75521	A2	19970528	HU 1996-2657	19950330 <--
	BR 9507251	A	19970902	BR 1995-7251	19950330 <--
	CN 1159161	A	19970910	CN 1995-193056	19950330 <--
	JP 09511243	T2	19971111	JP 1995-525409	19950330 <--
	FI 9603831	A	19961129	FI 1996-3831	19960925 <--
	NO 9604089	A	19961107	NO 1996-4089	19960927 <--
	US 5756490	A	19980526	US 1996-718401	19961216 <--
	AU 9912127	A1	19990325	AU 1999-12127	19990115
	AU 722362	B2	20000803		
PRAI	DE 1994-4411585	A	19940330		
	DE 1994-441585	A	19940330		
	AU 1995-20735	A3	19950330		
	WO 1995-EP1190	W	19950330		

TI Estrogen-gestagen combination for hormonal **contraception**

PI DE 4411585 A1 **19951005**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 4411585	A1	19951005	DE 1994-4411585	19940330 <--
WO 9526730	A1	19951012	WO 1995-EP1190	19950330 <--

W: AU, BG, BR, CA, CN, CZ, EE, FI, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RO, RU, SI, SK, UA, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9520735	A1	19951023	AU 1995-20735	19950330 <--
EP 750501	A1	19970102	EP 1995-913171	19950330 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

HU 75521	A2	19970528	HU 1996-2657	19950330 <--
BR 9507251	A	19970902	BR 1995-7251	19950330 <--
CN 1159161	A	19970910	CN 1995-193056	19950330 <--
JP 09511243	T2	19971111	JP 1995-525409	19950330 <--
FI 9603831	A	19961129	FI 1996-3831	19960925 <--
NO 9604089	A	19961107	NO 1996-4089	19960927 <--
US 5756490	A	19980526	US 1996-718401	19961216 <--
AU 9912127	A1	19990325	AU 1999-12127	19990115
AU 722362	B2	20000803		

AB An oral **contraceptive** system comprises a series of 23-24 daily dosage units contg. an estrogen and an ovulation-inhibiting amt. of a gestagen, to be followed by a series of 4-10 daily dosage units contg. an estrogen alone. The dosages are such as to minimize the estrogen and total hormone contents of each dosage unit while maintaining high **contraceptive** effectiveness and menstrual cycle control with low incidence of follicle development and side effects. Typical daily dosages are 1.0-4.0 mg 17.beta.-estradiol valerate and 0.05-0.075 mg Gestoden.

ST estrogen gestagen oral **contraceptive**

IT Estrogens
Progestogens
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen-gestagen combination for hormonal **contraception**)

IT **Contraceptives**
(female, estrogen-gestagen combination for hormonal **contraception**)

IT 50-28-2, 17.beta.-Estradiol, biological studies **57-63-6**, Ethynylestradiol 68-22-4, Norethisterone 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 979-32-8, 17.beta.-Estradiol valerate 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene **67392-87-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen-gestagen combination for hormonal **contraception**)

L9 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB Effective ovarian suppression is obtained in women of child-bearing age by
daily administration for 23 or 24 days, beginning on the 1st day of menstruation, of a compn. contg. (1) an estrogen selected from 17.beta.-estradiol (2.0-6.0 mg) and ethynylestradiol (0.015-0.020 mg) and (2) a gestagen selected from gestodene (0.05-0.075 mg), levonorgestrel (0.075-0.125 mg), desogestrel (0.06-0.15 mg), 3-ketodesogestrel (0.06-0.15
mg), **drospirenone** (0.1-0.3 mg), cyproterone acetate (0.1-0.2 mg), norgestimate (0.2-0.3 mg), and norethisterone (>0.35-0.75 mg), followed by 5 or 4 days of no or placebo medication. This course of treatment decreases the incidence of follicle maturation, recruitment of dominant follicles during the shortened medication-free period, and endogenous secretion of 17.beta.-estradiol.

AN 1995:696261 CAPLUS
DN 123:65882
TI Low-dose **contraceptive** composition containing estrogen and gestagen
PA Schering A.-G., Germany
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4344462	A1	19950629	DE 1993-4344462	19931222 <--
	DE 4344462	C2	19960201		
	US 5583129	A	19961210	US 1994-268996	19940630 <--
	WO 9517194	A1	19950629	WO 1994-EP4274	19941222 <--
	W: CA, CN, CZ, HU, JP, KR, LT, LV, NO, NZ, PL, RU, SI, SK, UA				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2179728	AA	19950629	CA 1994-2179728	19941222 <--
	EP 735883	A1	19961009	EP 1995-905574	19941222 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1142185	A	19970205	CN 1994-194888	19941222 <--
	HU 74877	A2	19970228	HU 1996-1750	19941222 <--
	NO 9602676	A	19960822	NO 1996-2676	19960624 <--
	US 5824667	A	19981020	US 1996-742147	19961031 <--
PRAI	DE 1993-4344462		19931222		
	US 1994-268996		19940630		
	WO 1994-EP4274		19941222		

TI Low-dose **contraceptive** composition containing estrogen and gestagen
PI DE 4344462 A1 **19950629**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4344462	A1	19950629	DE 1993-4344462	19931222 <--
	DE 4344462	C2	19960201		
	US 5583129	A	19961210	US 1994-268996	19940630 <--
	WO 9517194	A1	19950629	WO 1994-EP4274	19941222 <--
	W: CA, CN, CZ, HU, JP, KR, LT, LV, NO, NZ, PL, RU, SI, SK, UA				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2179728	AA	19950629	CA 1994-2179728	19941222 <--
	EP 735883	A1	19961009	EP 1995-905574	19941222 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1142185	A	19970205	CN 1994-194888	19941222 <--
	HU 74877	A2	19970228	HU 1996-1750	19941222 <--
	NO 9602676	A	19960822	NO 1996-2676	19960624 <--
	US 5824667	A	19981020	US 1996-742147	19961031 <--

AB Effective ovarian suppression is obtained in women of child-bearing age by
daily administration for 23 or 24 days, beginning on the 1st day of menstruation, of a compn. contg. (1) an estrogen selected from

17.beta.-estradiol (2.0-6.0 mg) and ethynylestradiol (0.015-0.020 mg) and (2) a gestagen selected from gestodene (0.05-0.075 mg), levonorgestrel (0.075-0.125 mg), desogestrel (0.06-0.15 mg), 3-ketodesogestrel (0.06-0.15 mg), **drospirenone** (0.1-0.3 mg), cyproterone acetate (0.1-0.2 mg), norgestimate (0.2-0.3 mg), and norethisterone (>0.35-0.75 mg), followed by 5 or 4 days of no or placebo medication. This course of treatment decreases the incidence of follicle maturation, recruitment of dominant follicles during the shortened medication-free period, and endogenous secretion of 17.beta.-estradiol.

ST **contraceptive** estrogen gestagen

IT Estrogens
Progestogens
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-dose **contraceptive** compn. contg. estrogen and gestagen)

IT **Contraceptives**
(female, low-dose **contraceptive** compn. contg. estrogen and gestagen)

IT 50-28-2, Estradiol, biological studies **57-63-6**, Ethynylestradiol 68-22-4, Norethisterone 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene **67392-87-4**, **Drospirenone**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-dose **contraceptive** compn. contg. estrogen and gestagen)

L9 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB The invention relates to a prepn. for substitution therapy and **contraception** comprising at least one progestogen and at least one estrogen in which the estrogen dose varies with a periodicity such that blood loss is substantially avoided, wherein the periodicity is preferably .ltoreq.10 days, more preferably .ltoreq.7 days, such as prepns. contg. the progestogen and/or estrogen in an oral, transdermal, parenteral and/or implantable application form. A tablet A contg. ethinyl estradiol 15, estradiol valerianate 1, and norethisterone 1 mg and a tablet B contg. 1.5 mg norethisterone were alternatingly administered with a periodicity of 4-7 days and an amenorrhea was induced without blood loss.

AN 1995:559955 CAPLUS

DN 122:283164

TI Progestogens and estrogens for substitution therapy and oral **contraception**

IN Koninckx, Philippe Robert Marie

PA Saturnus AG, Luxembourg

SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9507081	A1	19950316	WO 1994-EP2997	19940908 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	NL 9301562	A	19950403	NL 1993-1562	19930909 <--
	CA 2171460	AA	19950316	CA 1994-2171460	19940908 <--
	AU 9476952	A1	19950327	AU 1994-76952	19940908 <--

AU 708881 B2 19990812
EP 717626 A1 19960626 EP 1994-927583 19940908 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,
SE

CN 1133011 A 19961009 CN 1994-193713 19940908 <--
HU 74452 A2 19961230 HU 1996-592 19940908 <--
JP 09502194 T2 19970304 JP 1994-508461 19940908 <--
FI 9601098 A 19960403 FI 1996-1098 19960308 <--
US 5827843 A 19981027 US 1996-605118 19960604 <--
AU 9918488 A1 19990429 AU 1999-18488 19990226
PRAI NL 1993-1562 19930909
AU 1994-76952 19940908
WO 1994-EP2997 19940908

TI Progestogens and estrogens for substitution therapy and oral **contraception**

PI WO 9507081 A1 **19950316**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9507081	A1	19950316	WO 1994-EP2997	19940908 <--

PI W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ,
VN
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD,

TG

NL 9301562 A 19950403 NL 1993-1562 19930909 <--
CA 2171460 AA 19950316 CA 1994-2171460 19940908 <--
AU 9476952 A1 19950327 AU 1994-76952 19940908 <--
AU 708881 B2 19990812
EP 717626 A1 19960626 EP 1994-927583 19940908 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,
SE

CN 1133011 A 19961009 CN 1994-193713 19940908 <--
HU 74452 A2 19961230 HU 1996-592 19940908 <--
JP 09502194 T2 19970304 JP 1994-508461 19940908 <--
FI 9601098 A 19960403 FI 1996-1098 19960308 <--
US 5827843 A 19981027 US 1996-605118 19960604 <--
AU 9918488 A1 19990429 AU 1999-18488 19990226

AB The invention relates to a prepn. for substitution therapy and **contraception** comprising at least one progestogen and at least one estrogen in which the estrogen dose varies with a periodicity such that blood loss is substantially avoided, wherein the periodicity is preferably .ltoreq.7 days, such as prepns. contg. .ltoreq.10 days, more preferably .ltoreq.7 days, such as prepns. contg. the progestogen and/or estrogen in an oral, transdermal, parenteral and/or implantable application form. A tablet A contg. ethinyl estradiol 15, estradiol valerianate 1, and norethisterone 1 mg and a tablet B contg. 1.5 mg norethisterone were alternatingly administered with a periodicity of 4-7 days and an amenorrhea was induced without blood loss.

ST progestogen estrogen **contraceptive** amenorrhea induction

IT Amenorrhea
(progestogens and estrogens for substitution therapy and **contraception**)

IT Progestogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestogens and estrogens for substitution therapy and **contraception**)

IT Estrogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, progestogens and estrogens for substitution therapy and **contraception**)

IT Pharmaceutical dosage forms
(implants, progestogens and estrogens for substitution therapy and

contraception)

IT **Contraceptives**
Pharmaceutical dosage forms
(oral, progestogens and estrogens for substitution therapy and **contraception)**

IT Pharmaceutical dosage forms
(parenterals, progestogens and estrogens for substitution therapy and **contraception)**

IT Pharmaceutical dosage forms
(transdermal, progestogens and estrogens for substitution therapy and **contraception)**

IT 50-28-2, Estradiol, biological studies 51-98-9, Norethisterone acetate **57-63-6, Ethinylestradiol** 57-83-0, Progesterone, biological studies 71-58-9, Medroxyprogesterone acetate 427-51-0, Cyproterone acetate 797-63-7 979-32-8, Estradiol valerianate 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene **67392-87-4**, **Drospirenone**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestogens and estrogens for substitution therapy and **contraception)**

L9 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB Dihydrospirorenone (I) is a drug for the treatment of hormonal disturbances in premenopause (cycle stabilization), for hormonal substitution therapy in climacterium, for the treatment of androgen-induced disturbances, and as a **contraceptive** (no data). Formulation examples are given. I is preferably assocd. with an androgen.

AN 1991:423201 CAPLUS
DN 115:23201
TI Dihydrospirorenone as an antiandrogen
IN Beier, Sybille; Elger, Walter; Nishino, Yukishige; Wiechert, Rudolf
PA Schering A.-G., Fed. Rep. Ger.
SO Eur. Pat. Appl., 4 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 398460	A2	19901122	EP 1990-250127	19900516 <--
	EP 398460	A3	19910925		
	EP 398460	B1	19970702		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	DE 3916112	A1	19901122	DE 1989-3916112	19890516 <--
	DE 3916112	C2	19920430		
	CA 2016780	AA	19901116	CA 1990-2016780	19900515 <--
	HU 54500	A2	19910328	HU 1990-3045	19900515 <--
	HU 213408	B	19970630		
	DD 294417	A5	19911002	DD 1990-340683	19900515 <--
	AU 9055094	A1	19901122	AU 1990-55094	19900516 <--
	AU 642876	B2	19931104		
	CN 1047299	A	19901128	CN 1990-103713	19900516 <--
	CN 1033948	B	19970205		
	ZA 9003754	A	19910227	ZA 1990-3754	19900516 <--
	JP 03095121	A2	19910419	JP 1990-124308	19900516 <--
	JP 2848919	B2	19990120		
	IL 94416	A1	19970713	IL 1990-94416	19900516 <--
	AT 154881	E	19970715	AT 1990-250127	19900516 <--
	ES 2106728	T3	19971116	ES 1990-250127	19900516 <--
	US 5569652	A	19961029	US 1993-162387	19931207 <--
PRAI	DE 1989-3916112		19890516		
	US 1990-524396		19900516		
	US 1992-835000		19920214		

PI EP 398460 A2 **19901122**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 398460	A2	19901122	EP 1990-250127	19900516 <--
	EP 398460	A3	19910925		
	EP 398460	B1	19970702		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	DE 3916112	A1	19901122	DE 1989-3916112	19890516 <--
	DE 3916112	C2	19920430		
	CA 2016780	AA	19901116	CA 1990-2016780	19900515 <--
	HU 54500	A2	19910328	HU 1990-3045	19900515 <--
	HU 213408	B	19970630		
	DD 294417	A5	19911002	DD 1990-340683	19900515 <--
	AU 9055094	A1	19901122	AU 1990-55094	19900516 <--
	AU 642876	B2	19931104		
	CN 1047299	A	19901128	CN 1990-103713	19900516 <--
	CN 1033948	B	19970205		
	ZA 9003754	A	19910227	ZA 1990-3754	19900516 <--
	JP 03095121	A2	19910419	JP 1990-124308	19900516 <--
	JP 2848919	B2	19990120		
	IL 94416	A1	19970713	IL 1990-94416	19900516 <--
	AT 154881	E	19970715	AT 1990-250127	19900516 <--
	ES 2106728	T3	19971116	ES 1990-250127	19900516 <--
	US 5569652	A	19961029	US 1993-162387	19931207 <--

AB Dihydrospirorenone (I) is a drug for the treatment of hormonal disturbances in premenopause (cycle stabilization), for hormonal substitution therapy in climacterium, for the treatment of androgen-induced disturbances, and as a **contraceptive** (no data). Formulation examples are given. I is preferably assocd. with an androgen.

IT **Contraceptives**
(dihydrospirorenone)

IT **67392-87-4**, Dihydrospirorenone
RL: BIOL (Biological study)
(antiandrogen, for treatment of hormonal disturbances)

IT **57-63-6**, 17.alpha.-**Ethinylestradiol**
RL: BIOL (Biological study)
(hormonal disturbances treatment by dihydrospirorenone and)

L9 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2001 ACS

AB Oral formulations for **contraception** and treatment of gynecol. disorders consist of a mixt. of I [**67392-87-4**] (0.5-50 mg) and 17.alpha.-**ethinylestradiol** (II) [**57-63-6**] (0.03-0.05 mg) or other estrogens and the usual pharmaceutical carries. These formulations do not have neg. effects, such as blood pressure increase, assocd. with the conventional **contraceptives**. Thus, a mixt. of I 20, II 0.05, lactose 140-45, corn starch 59.5, aerosil 2, poly(vinylpyrrolidone) 25 and Mg stearate 0.5 mg was homogenized and pressed into tablets with each tablet weighing 225 mg.

AN 1982:110148 CAPLUS

DN 96:110148

TI Preparation for **contraception** and treatment of gynecological disorders

IN Elger, Walter; Beier, Sybille; Mannesmann, Gerda; Schillinger, Ekkehard

PA Schering A.-G. , Fed. Rep. Ger.

SO Ger. Offen., 9 pp.
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3022337	A1	19820107	DE 1980-3022337	19800611 <--
	DE 3022337	C2	19891019		

TI Preparation for **contraception** and treatment of gynecological disorders

PI DE 3022337 A1 **19820107**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3022337	A1	19820107	DE 1980-3022337	19800611 <--
	DE 3022337	C2	19891019		

AB Oral formulations for **contraception** and treatment of gynecol. disorders consist of a mixt. of I **[67392-87-4]** (0.5-50 mg) and 17.alpha.-**ethinylestradiol** (II) **[57-63-6]** (0.03-0.05 mg) or other estrogens and the usual pharmaceutical carries. These formulations do not have neg. effects, such as blood pressure increase, assocd. with the conventional **contraceptives**. Thus, a mixt. of I 20, II 0.05, lactose 140-45, corn starch 59.5, aerosil 2, poly(vinylpyrrolidone) 25 and Mg stearate 0.5 mg was homogenized and pressed into tablets with each tablet weighing 225 mg.

ST androstenone deriv estrogen **contraceptive**; spiroandrostanefuranone ethynylestradiol **contraceptive**

IT Estrogens
RL: BIOL (Biological study)
(**contraceptive** compns. contg. androstenone deriv. and)

IT **Contraceptives**
(spirodicyclopropaandrostenefuranone deriv. and estrogen combination)

IT **67392-87-4**
RL: BIOL (Biological study)
(**contraceptive** compns. contg. estrogens and)

IT **57-63-6**
RL: BIOL (Biological study)
(**contraceptive** compns. contg. spirodicyclopropaandrostenefura none deriv. and)

L9 ANSWER 16 OF 23 USPATFULL

AB 3-Oxyiminopregnane-21-carbolactones of formula I, ##STR1## wherein R is as defined by the specification, their production and use as pharmaceutical agents are described.

AN 2001:10878 USPATFULL

TI Oxyiminopregnancarbolactones

IN Laurent, Henry, Berlin, Germany, Federal Republic of
Lipp, Ralph, Berlin, Germany, Federal Republic of
Esperling, Peter, Berlin, Germany, Federal Republic of
Tack, Johannes-Wilhelm, Berlin, Germany, Federal Republic of

PA Schering Aktiengesellschaft, Germany, Federal Republic of (non-U.S. corporation)

PI	US 6177416	B1	20010123	<--
	WO 9824801	19980611		
AI	US 1999-308992		19991005 (9)	
	WO 1997-EP6657		19971201	
			19991005 PCT 371 date	
			19991005 PCT 102(e) date	
PRAI	DE 1996-19651000		19961201	
	US 1997-34997		19970107 (60)	

DT Utility
FS Granted
EXNAM Primary Examiner: Badio, Barbara
LREP Millen, White, Zelano & Branigan, P.C.
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 463
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI	US 6177416	B1	20010123	<--
	WO 9824801	19980611		

SUMM The 3-keto compound of formula II (**drospirenone**) that is analogous to the compounds of general formula I ##STR3##

SUMM c) a strong antiandrogenic action, and this at a dosage that is sufficient for **contraception** (DE-A 39 16 112).

SUMM **Drospirenone** is the first synthetic gestagen which, like natural progesterone, exhibits all three partial actions a), b), and c),

in a common dose range, but unlike progesterone is also bio-available in
a relevant amount after oral administration. **Drospirenone** can therefore be used either by itself or preferably in combination preparations together with an estrogen for hormonal **contraception** and/or for hormone replacement therapy. Owing to the antimineralocorticoids and antiandrogenic partial action, these preparations are also suitable for users. . .

SUMM The required daily dose of **drospirenone** for **contraception** or hormone replacement therapy is 1 to 10 mg.

SUMM . . . by so-called implants of hormonal active ingredients has been of great interest for hormone replacement therapy and recently also for **contraception** (Te-Yen Chien et al., "Transdermal **Contraceptive** Delivery System: Preclinical Development and Clinical Assessment" in Drug Development and Industrial Pharmacy, 20(4), 633-664 (1994)).

SUMM To date, **drospirenone**'s disadvantageous physicochemical substance properties, such as, e.g., low solubility in organic polymers, has hampered reasonable use of it via the. . .

SUMM The object of this invention therefore consists in converting **drospirenone** into derivatives that are to have considerably improved physicochemical substance properties, without the very advantageous pharmacological profile being significantly altered.

SUMM It has now been found that this can be achieved by converting **drospirenone** into the 3-oxime derivative (R=H) or the corresponding O-acyl derivative (R=acyl) of general formula I. The derivatives of general formula I are distinguished by, surprisingly enough, several times greater solubility than. **drospirenone** in organic polymers, which are suitable as skin contact adhesives, such as, e.g., polyacrylates, silicone adhesives, synthetic rubber). In the. . . general formula I from the matrix in an amount that can ensure an adequate transdermal flow of the active compound (**drospirenone**) or else its prodrug (compound of general formula I). This is in turn a prerequisite for a more relevant active. . .

SUMM The compounds thus are the first to actually make it possible to take full advantage of the **contraceptive** or therapeutic action of **drospirenone** after transdermal administration of a prodrug. Just like **drospirenone** itself, they can also be given orally, however.

SUMM **Contraceptively** effective 3-oximes and O-acylates have already been described in the 19-nortestosterone series. Levonorgestrel-oxime-17-acetate has been on the OC market for some years as a combination preparation with **ethinylestradiol** (DE 16 18 752, DE 16 20 102, DE 26 33 210, U.S. Pat. No. 3,780,073, U.S. Pat. No. 4,027,019,. . .

SUMM The production of the compounds of formula I is characterized in that the compound of formula II (**drospirenone**) ##STR4##

SUMM The oxime of general formula I (i.e., R=H) is produced in the reaction of **drospirenone** with hydroxylamine-hydrochloride/pyridine as an (E,Z)-mixture with an (E,Z) ratio.apprxeq.4:1.

SUMM . . . parenterally, as well as orally. In combination with an estrogen, combination preparations can be obtained that can be used for **contraception** and with menopausal symptoms.

SUMM . . . compounds of general formula (I) can be used, for example, by themselves or in combination with estrogens in preparations for **contraception**. The new compounds, however, also open all other possible uses that are now known for gestagens (see, e.g., "Kontrazeption mit Hormonen [**Contraception** with Hormones]," Hans-Dieter Taubert and Herbert Kuhl, Georg Thieme Verlag Stuttgart--New York, 1995).

SUMM The gestagenic and estrogenic active ingredient components are preferably administered together in **contraception** preparations. In the case of oral administration, the daily dose is preferably administered one time.

SUMM As synthetic estrogens, **ethinylestradiol**, 14.alpha.,17.alpha.-ethano-1,3,5(10)-estratriene-3,17.beta.-diol (WO 88/01275), 14.alpha.,17.alpha.-ethano-1,3,5(10)-estratriene-3,16.alpha.,17.beta.-triol (WO 91/08219) or the 15,15-dialkyl derivatives of estradiol and of these especially the 15,15-dimethylestradiol can be mentioned. **Ethinylestradiol** is preferred as a synthetic estrogen.

SUMM The estratrien-3-amidosulfonates that recently became known (WO 96/05216 and WO 96/05217), derived from estradiol or **ethinylestradiol**, which are distinguished by low hapatic estrogeneity, are also suitable as estrogens for use together with the compounds of general. . .

SUMM The estrogen is administered in an amount that corresponds to that of 0.01 to 0.05 mg of **ethinylestradiol**.

SUMM . . . are distinguished by the additional use of a competitive progesterone antagonist (H. B. Croxatto and A. M. Salvatierra in Female **Contraception** and Male Fertility Regulation, ed. by Runnebaum, Rabe & Kiesel--Vol. 2, Advances in Gynecological and Obstetric Research Series, Parthenon Publishing. . .

CLM What is claimed is:

13. A **contraceptive** formulation comprising a composition according to claim 12, wherein the composition is formulated to provide a daily dose of 0.1-25. . .

. . . according to claim 16, wherein the estrogen is administered in a daily dose amount that corresponds to 0.01-0.05 mg of **ethinylestradiol**.

IT 106-31-0, Butyric anhydride 108-24-7, Acetic anhydride 123-62-6, Propionic anhydride 1680-36-0, Nonanoic anhydride 2051-49-2, Caproic anhydride 5470-11-1, Hydroxylammonium chloride **67392-87-4**, 3-Oxo-6.beta.,7.beta.:15.beta.,16.beta.-dimethylene-17.alpha.-pregn-4-en-21,17carbolactone
(prepn. of oxyiminopregnanecarbolactones for estrogen contg. medicines)

L9 ANSWER 17 OF 23 USPATFULL

AB The present invention describes a two-stage pharmaceutical combined preparation for hormonal **contraception** containing at least 30 daily unit doses, which preparation, in its first stage, comprises as hormonal active ingredient a combination of an oestrogen preparation and, in a dose that is at least sufficient to inhibit ovulation, a gestagen preparation, in single stage form and, in the second stage comprises as hormonal active ingredient an oestrogen preparation only, wherein the first stage comprises a minimum of 25 and a maximum of 77 daily discrete or continuous unit doses and the second stage comprises 5, 6 or 7 daily discrete or continuous unit doses, and wherein the total number of daily units is equal to the total number of days of the desired cycle of a minimum of 30 and a maximum of 84 days. This combined preparation, in the form of a monthly pack, which is used for female fertility control, permits as low as possible an oestrogen content in each individual unit dose and also has a low total hormone content per cycle of administration, with high **contraceptive** reliability, low incidence of follicle development, and satisfactory cycle control with reliable avoidance of intermediate bleeding as well as undesired side effects.

AN 2000:21243 USPATFULL

TI Pharmaceutical combined preparation, kit and method for hormonal **contraception**

IN Schmidt-Gollwitzer, Karin, Berlin, Germany, Federal Republic of

Klemann, Walter, Berlin, Germany, Federal Republic of
PA Schering AG, Germany, Federal Republic of (non-U.S. corporation)
PI US 6027749 20000222
WO 9701342 19970116
AI US 1998-981488 19980603 (8)
WO 1996-DE1192 19960627
19980603 PCT 371 date
19980603 PCT 102(e) date
PRAI DE 1995-19525017 19950628
DT Utility
FS Granted
EXNAM Primary Examiner: Spear, James M.
LREP Millen, White, Zelano & Branigan, P.C.
CLMN Number of Claims: 40
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 804
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Pharmaceutical combined preparation, kit and method for hormonal **contraception**
PI US 6027749 20000222
WO 9701342 19970116
AB The present invention describes a two-stage pharmaceutical combined preparation for hormonal **contraception** containing at least 30 daily unit doses, which preparation, in its first stage, comprises as hormonal active ingredient a combination. . . content in each individual unit dose and also has a low total hormone content per cycle of administration, with high **contraceptive** reliability, low incidence of follicle development, and satisfactory cycle control with reliable avoidance of intermediate bleeding as well as undesired. . .
SUMM The present invention relates to a two-stage pharmaceutical combined preparation for hormonal **contraception** containing at least 30 daily unit doses, which preparation, in its first stage, comprises as hormonal active ingredient a combination. . . desired cycle of a minimum of 30 and a maximum of 84 days, and relates also to a corresponding pack (**contraceptive** kit) containing that combined preparation, and to a **contraceptive** method that uses the above **contraceptive** preparation.
SUMM Oral **contraceptives** in the form of combined preparations have been known since 1960 as so-called monophase preparations. Those preparations consist of 21. . .
SUMM As a result of the development of new, more active gestagens than those contained in the first oral **contraceptives**, a continuous reduction of the daily dose of gestagen has been possible. It has also been possible for the daily dose of oestrogen to be reduced although, as before, the oestrogen contained in hormonal **contraceptives** is usually ethynyloestradiol. In the development of new, improved oral **contraceptives**, the following three factors have been (and are) dominant:
SUMM (1) **contraceptive** reliability
SUMM The **contraceptive** reliability is effected in particular by the gestagenic component. The daily dosage amount of that component corresponds at least to. . .
SUMM The aim of the development of new oral **contraceptives** having a reduced daily hormone dose is to minimize the side effects described in epidemiological studies. More recent epidemiological data. . . point towards a trend for the improved tolerability of low-dose preparations in respect of cardiovascular side effects [Thorogood M, Oral **Contraceptives** and Cardiovascular Disease: an Epidemiologic Overview; Pharmacoepidemiology and Drug Safety, Vol. 2: 3-16 (1993); Gerstman B. B., Piper J. M., Tomita D. K., Ferguson W. J., Stadel B. V., Lundin F. E.; Oral **Contraceptive** Estrogen Dose and the Risk of Deep Venous Thromboembolic Disease, Am. J. E., Vol.133, No. 1, 32-36 (1991); Lidegaard O., Oral **contraception** and the risk of a

cerebral thromboembolic attack: results of a case-control study; BMJ Vol. 306, 956-63 (1993); Vessey M., Mant D., Smith A., Yeates D., Oral **contraceptives** and venous thromboembolism: findings in a large prospective study; BMJ, Vol. 292 (1986); Mishell D. R., Oral **Contraception**: Past, Present and Future Perspectives; Int. J. Fertil., 36 Suppl., 7-18 (1991)].

SUMM . . . detected by ultrasound examinations and hormone tests [Lunell N. O., Carlstrom K., Zador G., Ovulation inhibition with a combined oral **contraceptive** containing 20 .mu.g ethynyloestradiol and 250 .mu.g levonorgestrel; Acta Obstet. Gynecol. Scand. Suppl. 88: 17-21 (1979); Mall-Haefeli M., Werner-Zodrow I.,. . . Geburtsh. and Frauenheilk. 51, 35-38, Georg Thieme Verlag, Stuttgart-New York (1991); Strobel E., Behandlung mit oralen Kontrazeptiva (Treatment with oral **contraceptives**); Fortschr. Med. 110 Jg. No. 20 (1992); Letter to Editor, **Contraception** 45: 519-521 (1992); Teichmann A. T., Brill K., Can Dose Reduction of Ethynylestradiol in OCs Jeopardize Ovarian Suppression and Cycle. . .

SUMM . . . responsible for breakthrough ovulation (Chowdry et al., "Escape" ovulation in women due to the missing of low dose combination oral **contraceptive** pills, **Contraception**, 22: 241-247, 1980; Molloy B. G. et al., "Missed pill" conception: fact or fiction? Brit. Med. J. 290, 1474-1475, 1985). The **contraceptive** protection is consequently placed in question. The risk of a pregnancy is therefore high especially in the case of mistakes. . .

SUMM DE-OS 43 13 926 describes a pharmaceutical preparation for **contraception** having a minimum of four phases, which preparation consists of a fixed or sequential combination, consisting of a minimum of. . .

SUMM Common to all preparations for hormonal **contraception** on the market so far is that the pack unit is set to a 28-day cycle of administration (4-week rhythm).. . .

SUMM It has, of course, already been known for a long time that the onset of menstruation, when taking an oral **contraceptive** where there is a continuous daily administration of both oestrogen-containing and especially gestagen-containing unit doses, can be deferred until completion of the administration of the gestagen-containing unit doses [Hamerlynck J. V. Th. H. et al., **Contraception** 35,3: 199-205 (1987); Luodon N. B., IPPF Med. Bull. 13,1: 2-3 (1979); Luodon N. B. et al., Brit. Med. J.. . .

SUMM . . . the same time also a low total hormone content per cycle of administration, with which, with a high degree of **contraceptive** reliability, as low as possible an incidence of follicle development even in the first cycle of administration, and satisfactory cycle. . .

SUMM . . . the provision of the two-stage combined preparation described at the outset and also a corresponding pack containing that combined preparation (**contraceptive** kit) and a **contraceptive** method that uses the described **contraceptive** preparation.

SUMM The present invention relates furthermore to a **contraceptive** kit containing a minimum of 30 and a maximum of 84 daily unit doses each comprising at least one hormonal. . .

SUMM Preferred **contraceptive** kits according to the present invention are characterised as follows:

SUMM In a further embodiment of the **contraceptive** kit according to the invention, some of the unit doses of the first stage are arranged in periodically repeating sub-units. . .

SUMM In the case of the **contraceptive** method according to the invention, which employs the described combined preparation, in the first stage, commencing with the first day. . .

SUMM . . . with the combined preparation of the present invention follicle development can be suppressed and consequently breakthrough ovulations avoided, thereby increasing **contraceptive** reliability. This is

of great importance especially where mistakes are made in administration, particularly in the case of hormonal **contraceptives** having a low daily dose of ethynyloestradiol. Since 25% of women who take the pill are known to make mistakes. . . daily administration of two unit doses to more than 24 hours) (Finlay

I. G., Scott M. B. G.: Patterns of **contraceptive** pill-taking in an inner city practice. Br. Med. J. 1986, 293: 601-602), the combined preparation according to the invention, when used as an ovulation-inhibiting agent, increases **contraceptive** reliability. This is true in particular in the case of the lowest-dose preparations.

SUMM A variable manipulation of the initiation of the withdrawal bleeding is possible with the **contraceptive** kit according to the present invention, in which the unit doses of the first stage, at the earliest from the. . .

SUMM The **contraceptive** kit according to the invention is constructed, for example, in the form of a blister in which each individual segment,. . .

DETD . . . lower frequency of follicle development in the user. This means a lower risk of breakthrough ovulation and consequently a greater **contraceptive** reliability especially where mistakes are made in administration.

DETD . . . combined preparation according to the invention is effected in a manner completely analogous to that already known for conventional oral **contraceptives** having a 21-day administration period of active ingredients, such as, for example, Femovan.RTM. (ethynyloestradiol/gestodene) or Microgynon.RTM. (ethynyloestradiol/levonorgestrel). The formulation of. . .

DETD . . . in "Arzneimittelforschung" (Drug Research) 27, 2a, 296-318 (1977) and in "Aktuelle Entwicklungen in der hormonal Kontrazeption" (Current developments in hormonal **contraception**), H. Kuhl in "Gynacologe" 25: 231-240 (1992).

CLM What is claimed is:

1. Two-stage pharmaceutical combined preparation for hormonal **contraception** containing at least 30 daily unit doses, which preparation, in its first stage, comprises as hormonal active ingredient a combination. . .

11. **Contraceptive** kit containing at least 30 daily unit doses each containing at least one hormonal active ingredient, having a first and. . .

12. **Contraceptive** kit according to claim 11, wherein the first stage comprises 25 or 26 daily unit doses.

13. **Contraceptive** kit according to claim 11, wherein the first stage comprises a minimum of 28 and a maximum of 77 daily. . .

14. **Contraceptive** kit according to claim 13, wherein the first stage comprises 28 daily unit doses.

15. **Contraceptive** kit according to claim 13, wherein the first stage comprises 28 plus 7, or 28 plus a multiple of 7,. . .

16. **Contraceptive** kit according to claim 11, wherein the second stage comprises 7 daily unit doses.

17. **Contraceptive** kit according to claim 12, wherein the second stage comprises 5 or 6 daily unit doses, so that the kit. . .

18. **Contraceptive** kit according to claim 11, wherein the oestrogen of the first stage is selected from the group of compounds 17.beta.-oestradiol,. . .

19. **Contraceptive** kit according to claim 11, wherein the oestrogen of the first stage is contained in each daily unit dose in.

20. **Contraceptive** kit according to claim 11, wherein there is contained in each daily unit dose in the second stage an amount. . .

21. **Contraceptive** kit containing at least 30 daily unit doses each containing at least one hormonal active ingredient, having a first and. . .

22. **Contraceptive** kit according to claim 21, wherein the unit doses are arranged in sub-units at the earliest from the 26th daily. .

23. **Contraceptive** kit according to claim 21, wherein the individual sub-units can be separated from one another by perforations or other means. . .

24. **Contraceptive** kit according to claim 21, wherein the separate sub-units each contain 7 unit doses.

25. **Contraceptive** kit according to claim 21, wherein the first stage comprises 28 plus 7, or 28 plus a multiple of 7,. . .

26. **Contraceptive** kit according to claim 21, wherein the second stage comprises 7 daily unit doses.

27. **Contraceptive** kit according to claim 21, wherein the oestrogen of the first stage is selected from the group of compounds 17.beta.-oestradiol,. . .

28. **Contraceptive** kit according to claim 21, wherein the oestrogen of the first stage is contained in each daily unit dose in.

29. **Contraceptive** kit according to claim 21, wherein there is contained in each daily unit dose in the second stage an amount. . .

30. Method of **contraception** in female mammals comprising a sequential administration for a minimum of 30 and a maximum of 84 days of daily. . .

IT 50-28-2, 17.beta.-Estradiol, biological studies **57-63-6**, Ethynylestradiol 68-22-4, Norethisterone 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 979-32-8, 17.beta.-Estradiol valerate 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene **67392-87-4** (contraceptive hormonal combination, kit, and method)

L9 ANSWER 18 OF 23 USPATFULL

AB The invention relates to a preparation for substitution therapy and oral **contraception** comprising at least one progestogen and at least one estrogen in which the estrogen dose varies with a periodicity such that blood loss is substantially avoided, wherein the periodicity is preferably less than 10 days, more preferably less than 7 days, such as preparations containing the progestogen and/or estrogen in an oral, transdermal, parenteral and/or implantable application form.

AN 1998:131711 USPATFULL

TI Preparation for substitution therapy, containing at least one progestogen and at least one estrogen

IN Koninckx, Philippe Robert Marie Wilhelmus Ghislain, Bierbeek, Belgium

PA Saturnus A.G., Luxembourg, Germany, Federal Republic of (non-U.S. corporation)

PI US 5827843 19981027 <--
WO 9507081 19950316 <--

AI US 1996-605118 19960604 (8)
WO 1994-EP2997 19940908
19960604 PCT 371 date
19960604 PCT 102(e) date

PRAI NL 1993-1562 19930909

DT Utility

FS Granted

EXNAM Primary Examiner: Fay, Zohreh

LREP Webb Ziesenheim Bruening Logsdon Orkin & Hanson, P.C.

CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 250
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5827843 19981027 <--
WO 9507081 19950316 <--
AB The invention relates to a preparation for substitution therapy and oral **contraception** comprising at least one progestogen and at least one estrogen in which the estrogen dose varies with a periodicity such. . .
SUMM The present invention relates to a preparation for substitution therapy and for oral **contraception**. More particularly the present invention on the one hand relates to relieving the effects which occur because the ovaries decrease. . .
SUMM On the other hand, the present invention relates to preparations designed for oral **contraception** with substantially continuous application.
SUMM In continuous application of oral **contraceptive** frequently intermediate bleedings occur. The preparations according to the present invention are designed to induce menstrual bleeding with a regular. . .
SUMM EP-A-559 240 discloses preparations for substitution therapy and oral **contraception** in which the estrogen dose is constant and the progestagen dose is periodically alternated.
SUMM The invention therefore relates to a preparation for substitution therapy and for oral **contraception** comprising at least one progestogen and at least one estrogen in which the estrogen dose varies with a periodicity such. . .
SUMM The preparations for oral **contraceptive** comprise estrogens and progestogens in common form.
SUMM Using the preparations according to the invention as oral **contraceptive** intermediate bleeding will be substantially reduced.
DETD A preparation according to the invention for oral **contraceptive** with optimal cycle control comprises tablets of type A comprising 20 .mu.g aethinyl-estradiol and 75 .mu.g gestoden. The preparation contained. . .
DETD A preparation according to the invention for oral **contraceptive** with optimal cycle control comprises tablets of type A comprising 15 .mu.g aethinyl-estradiol and 75 .mu.g gestoden, and tablets of. . .
DETD A preparation for oral **contraceptive** according to the invention comprises tablets of type A comprising 20 .mu.g aethinyl-estradiol and 75 .mu.g gestoden, and tablets of. . .
DETD . . . to the actual and the above mentioned combinations of estrogens and progestagens in products for hormone replacement therapy and for **contraception**.
CLM What is claimed is:
1. Preparation for substitution therapy and for oral **contraception** comprising at least one progestogen and at least one estrogen having dosing means in association therewith wherein the progestogen dose. . .
IT 50-28-2, Estradiol, biological studies 51-98-9, Norethisterone acetate **57-63-6**, Ethinylestradiol 57-83-0, Progesterone, biological studies 71-58-9, Medroxyprogesterone acetate 427-51-0, Cyproterone acetate 797-63-7 979-32-8, Estradiol valerianate 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene **67392-87-4**, Drospirenone (progestogens and estrogens for substitution therapy and contraception)

L9 ANSWER 19 OF 23 USPATFULL
AB A combination product for oral **contraception** is disclosed comprising an estrogen selected from

2.0 to 6.0 mg of 17.beta.-estradiol and

0.020 mg of **ethinylestradiol;**

and a gestagen selected from

0.25 to 0.30 mg of **drospirenone** and

0.1 to 0.2 mg of cyproterone acetate,

followed by 5 or 4 pill-free or sugar pill days.

AN 1998:128255 USPATFULL
TI Composition for **contraception**
IN Spona, Jurgen, Vienna, Austria
Dusterberg, Bernd, Berlin, Germany, Federal Republic of
Ludicke, Frank, Geneva, Switzerland
PA Schering Aktiengesellschaft, Germany, Federal Republic of (non-U.S. corporation) <--
PI US 5824667 19981020
AI US 1996-742147 19961031 (8)
RLI Continuation of Ser. No. US 1994-268996, filed on 30 Jun 1994, now patented, Pat. No. US 5583129
PRAI DE 1993-4344462 19931222
DT Utility
FS Granted
EXNAM Primary Examiner: Spivack, Phyllis G.
LREP Millen, White, Zelano & Branigan, P.C.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 349
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Composition for **contraception** <--
PI US 5824667 19981020
AB A combination product for oral **contraception** is disclosed comprising an estrogen selected from
AB 0.020 mg of **ethinylestradiol;**
AB 0.25 to 0.30 mg of **drospirenone** and
SUMM This invention relates to the common use of estrogens and gestagens for the production of a combination preparation for oral **contraception** and a corresponding pack containing this combination preparation.
SUMM Combination preparations for oral **contraception** are already known, for example, Femovan.RTM. [DE-PS 2 546 062] or Marvelon.RTM. [DE-OS 2 361 120]. These preparations consist of. . . placebos). The dose to be administered daily is uniformly high in each case (so-called single-phase preparations) and produces the desired **contraceptive** effect in the entire intake period and in the intake pause or during the intake of the placebos. In most. . .
SUMM . . . Pasquale) or completely (Kuhl) bridged over by estrogen-containing dosage units. In this case, it is possible that the synthetic estrogen **ethinylestradiol** otherwise contained in oral **contraceptives** is replaced partially or completely by a conjugated estrogen, preferably estradiol.
SUMM A combination preparation for substitution therapy and **contraception** for females before menopause (approximately starting from the 40th year of life) is known from EP-A-0 253 607. This combination. . .
SUMM **ethinylestradiol** and
SUMM . . . by the hormonal changeover of the female organism in this phase. Such a composition simultaneously assures a premenopausal female the **contraceptive** protection still necessary at this age.
SUMM The development of new oral **contraceptives** for females of reproductive age before premenopause was characterized during the last twenty years above all by the reduction of. . .

SUMM . . . the meantime confirm the desired trend toward better compatibility of lower-dosed preparations relative to cardiovascular complications [(1.) Thorogood, M., Oral **Contraceptives** and Cardiovascular Disease: An Epidemiologic Overview; Pharmacoepidemiology and Drug Safety, Vol. 2: 3-16 (1993); (2.) Gerstman, B. B.; Piper, J. M.; Tomita, D. K.; Ferguson, W. J.; Stadel, B. V.; Lundin, F. E.; Oral **Contraceptive** Estrogen Dose and the Risk of Deep Venous Thromboembolic Disease, Am. J. E., Vol. 133, No. 1, 32-36 (1991); (3.) Lidegaard, O., Oral **contraception** and risk of a cerebral thromboembolic attack: results of a case-control study; BMJ Vol. 306, 956-63 (1993); (4.) Vessey, M.; Mant, D.; Smith, A.; Yeates, D.; Oral **contraceptives** and venous thromboembolism: findings in a large prospective study; BMJ, Vol. 292, (1986); (5.) Mishell, D. R., Oral **Contraception**: Past, Present and Future Perspectives; Int. J. Fertil., 36 Suppl., 7-18 (1991)].

SUMM . . . above all between the level of the estrogen dose and the incidence of cardiovascular diseases. But the maintenance of the **contraceptive** effectiveness stands in the way of an extreme reduction of the daily estrogen dose. Although the ovulation-inhibiting effect of the low-dosed oral **contraceptives** is caused mainly by the gestagenic component, the estrogenic component also makes a significant contribution to the central inhibition action. . .

SUMM The lowest estrogen dose contained in an oral **contraceptive** on the market at this time is 20 .mu.g of **ethinylestradiol**, combined with 150 .mu.g of desogestrel (Mercilon). Although the cycle control of this preparation is, as expected, somewhat poorer in. . . But the observation, made identically in several studies, of a lesser ovarial suppression of the preparation containing 20 .mu.g of **ethinylestradiol** represents a clinically important problem. Obviously with this very low estrogen dose, in the case of many females, the maturation. . . ultrasonic studies or hormonal studies, results [(6.) Lunell, N. O.; Carlstrom, K.; Zador, G.; Ovulation inhibition with a combined oral **contraceptive** containing 20 .mu.g of **ethinylestradiol** and 250 .mu.g of levonorgestrel; Acta. Obstet. Gynecol. Scand. Suppl. 88: 17-21 (1979); (7.) Mall-Haefeli, M.; Werner-Zodrow, I.; Huber, P.. . . and Gynecology] 51, 35-38, Georg Thieme Verlag, Stuttgart-New York (1991); (8.) Strobel, E., Behandlung mit oralen Kontrazeptiva [Treatment with Oral **Contraceptives**]; Fortschr. Med. Vol. 110, No. 20 (1992); (9.) Letter to Editor, **Contraception** 45: 519-521 (1992); (10.) Teichmann, A. T.; Brill, K.; Can Dose Reduction of **Ethinylestradiol** in OCs Jeopardize Ovarian Suppression and Cycle Control? Abstract Book, VIIIth World Congress on Human Reproduction, Bali, Indonesia (1993)].

SUMM . . . The requirements for an ovulation would thus be present. It is estimated that approximately one third of females take oral **contraceptives** irregularly within one year of use (Gynpress, Volume 1, No. 3, 1990). The risk of a pregnancy is therefore high especially in the case of intake errors with the 20 .mu.g **ethinylestradiol** preparations.

DETD 0.015 to 0.020 mg of **ethinylestradiol**;

DETD 0.1 to 0.3 mg of **drospirenone**,

DETD for the production of a form of dosage for **contraception** for a female of reproductive age, who has not yet reached premenopause, by administration of the form of dosage for. . .

DETD 0.020 mg of **ethinylestradiol**;

DETD 0.25 to 0.30 mg of **drospirenone**,

DETD for the production of a form of dosage for **contraception** as described above.

DETD In addition, this invention relates to a combination product for oral **contraception**, which comprises

DETD 0.020 mg of **ethinylestradiol**;

DETD 0.25 to 0.30 mg of **drospirenone**,

DETD An especially preferred combination preparation according to this invention comprises 23 dosage units, each containing 20 .mu.g of

ethinylestradiol and 75 .mu.g of gestodene and 5 sugar pills or other indications to show that no dosage unit or a. . .

DETD The clinical study briefly described below was performed with **ethinylestradiol** as estrogen and gestodene as representative of the substance class of the gestagens possible according to the invention. All possible combinations of **ethinylestradiol** or estradiol according to the invention in the indicated dosages with one of the selected gestagens in the indicated dosages. . .

DETD The 23-day administration of 20 .mu.g of **ethinylestradiol** in combination with 75 .mu.g of gestodene results, in comparison to the 21-day administration, in a stronger ovarian suppression. In. . .

DETD . . . according to the invention thus achieves the effectiveness previously known for preparations with a daily content of 30 .mu.g of **ethinylestradiol**, although the daily **ethinylestradiol** dose is 33% lower and also the total dose per cycle is 27% lower.

DETD The advantages of a combination preparation for oral **contraception** to be administered over 23 days relative to the usual 21-day preparations with less than 30 .mu.g of **ethinylestradiol** can be characterized as follows:

DETD . . . the 23-day preparation relative to a maximum of 40% among those who received the 21-day preparation). This means a greater **contraceptive** reliability of the 23-day preparation, especially in the case of previous intake errors. The danger of "breakthrough ovulations" is smaller.

DETD In summary, an intake, extended by two (or three) days, of preparations containing 20 .mu.g of **ethinylestradiol** in each daily dosage unit can produce the above-mentioned advantages, without the daily dose having to be raised to the previously largely used level of 30 .mu.g of **ethinylestradiol**.

DETD . . . for a combination preparation according to the invention takes place completely analogously as it is already known for usual oral **contraceptives** with 21-day intake period of the active ingredients, such as, for example, Femovan.RTM. (**ethinylestradiol**/gestodene) or Microgynon.RTM. (**ethinylestradiol**/levonorgestrel).

DETD A pack containing a combination preparation according to the invention is also designed analogously to packs for already known oral **contraceptives** on the market with the variation that instead of the usual 21 dosage units containing the active components, now 23. .

.

DETD . . . the statements made in EP-A 0 253 607, especially also to the statements there for determination of equivalent amounts of **ethinylestradiol** and 17.beta.-estradiol, on the one hand, and various gestagens, such as levonorgestrel, desogestrel, 3-ketodesogestrel and gestodene, on the other hand.

DETD . . . Agent Research) 27, 2a, 296-318 (1977), as well as to "Aktuelle Entwicklungen in der hormonalen Kontrazeption" [Current Developments in Hormonal **Contraception**]; H. Kuhl in Gynakologe" [Gynecologist) 25: 231-240 (1992).

DETD FIG. 1: Area with the 17.beta.-estradiol level in groups of 30 females, who are treated with an oral **contraceptive** (75 .mu.g of gestodene+20 .mu.g of **ethinylestradiol**) in 21- or 23-day administration interval over three cycles.

DETD . . . Number of females in %, who showed follicular developments (>13 mm diameter) with 21- or 23-day treatment with an oral **contraceptive** (75 .mu.g of gestodene+20 .mu.g of **ethinylestradiol**).

CLM What is claimed is:

1. A combination product for oral **contraception**, comprising (a) 23 or 24 dosage units, each containing an estrogen selected from >2.0 to 6.0 mg of 17.beta.-estradiol and 0.020 mg of **ethinylestradiol**; and a gestagen selected from 0.25 to 0.30 mg of **drospirenone** and 0.1 to 0.2 mg of cyproterone acetate, and

b) 5 or 4, respectively, active ingredient-free placebo pills or other.

. .

2. A combination preparation for oral **contraception** according to claim 1, wherein the estrogen is **ethinylestradiol**.

4. A combination preparation of claim 2, wherein the gestagen is **drospirenone**.

5. A combination preparation according to claim 1, wherein the estrogen is present in a dose of 20 .mu.g of **ethinylestradiol** or an equivalent dose of 17.beta.-estradiol and the gestagen is present in a dose equivalent to 75 .mu.g of gestadene.

. . .

7. A combination preparation according to claim 1, which comprises 23 dosage units, each containing 20 .mu.g of **ethinylestradiol** and a dose of cyproterone acetate or **drospirenone** equivalent to 75 .mu.g of gestodene and 5 placebo pills or other indications to show that no dosage unit or. . .

10. A combination preparation of claim 8, wherein the gestagen is **drospirenone**.

IT 50-28-2, Estradiol, biological studies **57-63-6**, Ethynylestradiol 68-22-4, Norethisterone 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene **67392-87-4**, Drospirenone
(low-dose contraceptive compn. contg. estrogen and gestagen)

L9 ANSWER 20 OF 23 USPATFULL

AB A pharmaceutical combination preparation with two hormone components that are manufactured physically separately in a packaging unit and that are intended for time-sequential oral administration, which in each case consist of a number of daily dosage units that are placed physically separately and are individually removable in the packaging unit. As a hormonal active ingredient, a first hormone component contains in combination an estrogen preparation and, in at least a dosage that is sufficient to inhibit ovulation, a gestagen preparation, and as a hormonal active ingredient the second hormone component contains only an estrogen preparation. The first hormone component comprises 23 or 24 daily units and the second hormone component comprises 4 to 10 daily units. The total number of hormone daily units is equal to the total number of days of the desired cycle, but at least 28 days in length. This combination preparation is used for female birth control, and allows for an estrogen content that is as low as possible in each individual dosage unit and also has a low total hormone content per administration cycle, with high **contraceptive** reliability, low incidence of follicular development, and satisfactory cycle control, with reliable avoidance of intracyclic menstrual bleeding as well as of undesirable side-effects.

AN 1998:57914 USPATFULL

TI Pharmaceutical combination preparation for hormonal **contraception**

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PI US 5756490 19980526
WO 9526730 19951012

AI US 1996-718401 19961216 (8)
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PRAI DE 1994-4411585 19940330
DT Utility
FS Granted
EXNAM Primary Examiner: Jordan, Kimberly
LREP Millen, White, Zelano & Branigan, P.C.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 502
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Pharmaceutical combination preparation for hormonal, **contraception** <--
PI US 5756490 19980526
WO 9526730 19951012
AB . . . as possible in each individual dosage unit and also has a low total hormone content per administration cycle, with high **contraceptive** reliability, low incidence of follicular development, and satisfactory cycle control, with reliable avoidance of intracyclic menstrual bleeding as well as. . .
SUMM Oral **contraceptives** in the form of combination preparations have been known as so-called one-phase preparations since 1960.
SUMM . . . dosage has been continuously reduced through the development of new, more effective gestagens than those contained in the first oral **contraceptives**. It was also possible to lower, the daily estrogen dosage, although in most cases **ethinylestradiol** is still contained as an estrogen in hormonal **contraceptives**.
SUMM Because of the development of new, improved oral **contraceptives**, the following three points were (and are) emphasized:
SUMM (1) **Contraceptive** reliability,
SUMM **Contraceptive** reliability is mainly provided by the gestagen component. The amount of its daily dosage corresponds in each case to at least the maximum dose that is considered necessary for the gestagen in question to inhibit ovulation. The **ethinylestradiol** that is used in most cases as an estrogen in combination preparations is supposed to. increase the ovulation-inhibiting effect of the gestagen and mainly to ensure cycle stability. The daily dose in the case of **ethinylestradiol** administered alone, which must be used to inhibit ovulation, is 100 .mu.g.
SUMM The purpose of the development of new oral **contraceptives** with a reduced daily hormone dose was to minimize the side- effects that are described in epidemiological studies. Recent epidemiological. . . data point to such a trend toward better compatibility of low-dosed preparations with respect to cardiovascular side-effects. [Thorogood M., Oral **Contraceptives** and Cardiovascular Disease: An Epidemiologic Overview; Pharmacoepidemiology and Drug Safety, Vol. 2: 3-16 (1993); Gerstman B. B., Piper J. M., Tomita D. K., Ferguson W. J., Stadel B. V., Lundin F. E.; Oral **Contraceptive** Estrogen Dose and the Risk of Deep Venous Thromboembolic Disease, Am J E Vol. 133, No. 1, 32-36 (1991); Lidegaard O., Oral **Contraception** and Risk of a Cerebral Thromboembolic Attack: Results of a Case-Control Study: BMJ Vol. 306, 956-63 (1993); Vessey M., Mant D., Smith A., Yeates D., Oral **Contraceptives** and Venous-Thromboembolism: Findings in a Large Prospective Study; BMJ, Vol. 292, (1986); Mishell D. R., Oral **Contraception**: Past, Present and Future Perspectives; Int J Fertile, 36 Suppl., 7-18 (1991)].
SUMM The preparation with the lowest-dosed amount of estrogen at this time is marketed as Mercilon.RTM. and contains 20 .mu.g of **ethinylestradiol** in combination with 150 .mu.g of desogestrel in each daily dosage unit over 21 days, followed by a 7-day pill-free. . . estrogen dose. The observation, confirmed in several studies, of

slighter ovarian suppression for the preparation that contains 20 .mu.g of **ethinylestradiol** represents another clinically important problem. Obviously, for many women this very low estrogen dose can result in the maturation of. . . detected in ultrasound studies or hormone studies [Lunell N. O., Carlstrom K., Zador G., Ovulation Inhibition with a Combined Oral **Contraceptive** Containing 20 .mu.g of **Ethinylestradiol** and 250 .mu.g of Levonorgestrel; Acta Obstet Gynecol Scand Suppl. 88: 17-21 (1979); Mall-Haefeli M., Werner-Zodrow I, Huber P. R.,. . . [Childbirth and Gynecology], 51, 35-38, Georg Thieme Verlag, Stuttgart-New York (1991); Strobel E., Behandlung mit oralen Kontrazeptiva [Treatment with Oral **Contraceptives**]; Fortschr. Med. 110 Jg. No. 20 (1992); Letter to Editor, **Contraception** 45: 519-521 (1992);

SUMM Teichmann A. T., Brill K., Can Dose Reduction of **Ethinylestradiol** in OCs Jeopardize Ovarian Suppression and Cycle Control? Abstract Book, VIIIth World Congress on Human Reproduction, Bali, Indonesia (1993)].

SUMM . . . be responsible for breakthrough ovulations (Chowdhury et al., "Escape" Ovulation in Women Due to the Missing of Low-Dose Combination Oral **Contraceptive** Pills, **Contraception**, 22: 241-247, 1980; Molloy B. G. et al., "Missed Pill" Conception: Fact or Fiction? Brit. Med. J. 290, 1474-1475, 1985). **Contraceptive** protection is thus jeopardized. The risk of pregnancy is therefore high, especially in the case of intake errors below the 20 .mu.g **ethinylestradiol** preparations.

SUMM From DE-PS 43 08 406 (not prepublished), an ovulation-inhibiting agent in the form of a combination preparation for **contraception** is already known, in which at least one hormone component that contains both estrogen and gestagen is provided, in which. . .

SUMM . . . possible in each individual dosage unit but also with a low total hormone content per administration cycle, whereby with high **contraceptive** reliability, an incidence of follicular development that is as low as possible and satisfactory cycle control with reliable avoidance of. . .

SUMM . . . can be suppressed as early as in the first intake cycle, and thus breakthrough ovulations can be avoided, thereby increasing **contraceptive** reliability.

SUMM This is of eminent importance mainly in the case of intake errors, namely especially with hormonal **contraceptives** with low daily **ethinylestradiol** dose amounts. Since, in the case of 25% of women who take the pill, intake errors (skipping dosage units or. . . of two dosage units to more than 24 hours) are known (Finlay I. G., Scott M. B. G.: Patterns of **Contraceptive** Pill-taking in an Inner City Practice. Br. Med. J. 1986, 293: 601-602), the combination preparation according to the invention, if it is used as an ovulation-inhibiting agent, increases **contraceptive** reliability. This is true especially in the case of lowest-dosed preparations.

SUMM **ethinylestradiol** and

SUMM **ethinylestradiol** and

SUMM 0.01 to 0.04 mg of **ethinylestradiol**,

SUMM . . . the daily amounts in the daily units of the first hormone component, 0.015 to 0.025 mg is especially preferred for **ethinylestradiol**, 1.0 to 4.0 mg is especially preferred for 17.beta.-estradiol valerate, and 0.05 to 0.075 mg is especially preferred for gestodene.

SUMM 0.002 to 0.04 mg of **ethinylestradiol**,

SUMM According to an especially preferred embodiment, the second hormone component in each daily dosage unit contains, as estrogen, **ethinylestradiol** in an amount of 0.01 to 0.025 mg, 17.beta.-estradiol in an amount of 1.0 to 3.0 mg, or 17.beta.-estradiol valerate. . .

SUMM As an estrogen for both the first and the second hormone component, primarily **ethinylestradiol** or 17.beta.-estradiol is considered.

DETD The combination preparation according to the invention is used in female **contraception** by administering the daily dosage units of the first hormone component over 23 or 24 days, beginning on day one. . . .

DETD . . . the invention that is administered over generally 28 days compared to the previously described preparations, especially those with a daily **ethinylestradiol** dose of less than 30 .mu.g and those with a pill-free interval, can be characterized as follows:

DETD . . . significantly lower frequency of follicular development in the user. This means a lower risk of breakthrough ovulation and thus greater **contraceptive** reliability, especially in the case of intake errors.

DETD . . . a combination preparation according to the invention is carried out completely analogously to the way already known for conventional oral **contraceptives** with a 21-day intake period of the active ingredients, such as, for example, Femovan.RTM. (**ethinylestradiol**/gestodene) or Microgynon.RTM. (**ethinylestradiol**/levonorogestrel). The formulation of the dosage units that contain only estrogen can also be carried out quite analogously to the way. . .

DETD . . . that contains a combination preparation according to the invention is also built up analogously to packings for already known oral **contraceptives** that are on the market, with the difference that, instead of the usual 21 dosage units that contain active components,. . .

DETD In addition, the invention relates to a process for female **contraception** in which the above-described combination preparation is administered in the indicated way.

DETD To determine equivalent-action amounts of **ethinylestradiol** and 17.beta.-estradiol, on the one hand, and various gestagens such as gestodene, levonorgestrel, desogestrel and 3-ketodesogestrel, on the other hand,. . . (Drug Research) 27, 2a, 296-318 (1977) as well as in "Aktuelle Entwicklungen in der hormonalen Kontrazeption [Current Developments in Hormonal **Contraception**]": H. Kuhl in "Gynakologe [Gynecologist]" 25: 231-240 (1992).

CLM What is claimed is:

. . . according to claim 1, wherein the estrogen of the first hormone component is selected from the group of compounds 17.beta.-estradiol, **ethinylestradiol** and 17.beta.-estradiol valerate and the gestagen is selected from the group of compounds gestodene, levonorgestrel, desogestrel, 3-ketodesogestrel, drospironenone, cyproterone acetate, norgestimate and norethisterone and the estrogen of the second hormone component is selected from the group of compounds 17.beta.-estradiol, **ethinylestradiol** and 17.beta.-estradiol valerate.

. . . daily dosage unit is contained in a dose of 1.0 to 6.0 mg of 17.beta.-estradiol, 0.015 to 0.025 mg of **ethinylestradiol**, and 1.0 to 4.0 mg of 17.beta.-estradiol valerate and the gestagen in each daily dosage unit is contained in a. . .

. . . contains, in each daily dosage unit, an amount of: 1.0 to 6.0 mg of 17.beta.-estradiol, 0.002 to 0.04 mg of **ethinylestradiol**, and 1.0 to 4.0 mg of 17.beta.-estradiol valerate.

. . . contains, in each daily dosage unit, an amount of 1.0 to 6.0 mg of 17.beta.-estradiol, 0.002 to 0.04 mg of **ethinylestradiol**, and 1.0 to 4.0 mg of 17.beta.-estradiol valerate.

6. Combination preparation according to claim 5, wherein the second hormone component in each daily dosage unit contains **ethinylestradiol** in an amount of 0.01 to 0.025 mg.

. . . contains, in each daily dosage unit, an amount of: 1.0 to 3.0 mg of 17.beta.-estradiol, 0.01 to 0.025 mg of **ethinylestradiol**, and 1.0 to 4.0 mg of 17.beta.-estradiol valerate.

. . . The combination preparation of claim 1, wherein the estrogen in both the first and second hormone components is selected from **ethinylestradiol** or 17.beta.-estradiol.

IT 50-28-2, 17.beta.-Estradiol, biological studies **57-63-6**, Ethynylestradiol 68-22-4, Norethisterone 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 979-32-8, 17.beta.-Estradiol valerate 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene **67392-87-4** (estrogen-gestagen combination for hormonal contraception)

L9 ANSWER 21 OF 23 USPATFULL

AB This invention provides a method of **contraception** which comprises administering to a female of child bearing age for 28 consecutive days,

a first phase combination of a progestin at a daily dosage equivalent in progestational activity to 40-125 .mu.g levonorgestrel and an estrogen at a daily dosage equivalent in estrogenic activity to 10-20 .mu.g ethinyl estradiol for 3-8 days beginning on day 1 of the menstrual cycle, wherein the same dosage of the progestin and estrogen combination is administered in each of the 3-8 days,

a second phase combination of a progestin at a daily dosage equivalent in progestational activity to 40-125 .mu.g levonorgestrel and an estrogen at a daily dosage equivalent in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the first phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 4-15 days,

a third phase combination of a progestin at a daily dosage equivalent in progestational activity to 40-125 .mu.g levonorgestrel and an estrogen at a daily dosage equivalent in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 4-15 days beginning on the day immediately following the last day of administration of the second phase combination, wherein the same dosage of the progestin and estrogen combination is administered in each of the 4-15 days, and

an estrogen phase estrogen at a daily dosage equivalent in estrogenic activity to 10-20 .mu.g ethinyl estradiol, for 3-5 days beginning on the day immediately following the last day of administration of the third phase combination, wherein the same dosage of the estrogen is administered in each of the 3-5 days,

provided that the daily dosage of the combination administered in the first phase is not the same as the daily dosage of the combination administered in the second phase and that the daily dosage of the combination administered in the second phase is not the same as the daily dosage of the combination administered in the third phase.

AN 1998:48398 USPATFULL

TI Oral **contraceptive**

IN Gast, Michael J., Phoenixville, PA, United States

PA American Home Products Corporation, Madison, NJ, United States (U.S. corporation)

PI US 5747480 19980505 <--

AI US 1997-839286 19970417 (8)
PRAI US 1996-17092 19960508 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Weddington, Kevin E.
LREP Milowsky, Arnold S.
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 818
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Oral **contraceptive** <--
PI US 5747480 19980505
AB This invention provides a method of **contraception** which comprises administering to a female of child bearing age for 28 consecutive days,
SUMM The vast majority of oral **contraceptives** consist of a combination of a progestin and estrogen that are administered concurrently for 21 days followed either by a. . . administration of a placebo for 7 days in each 28 day cycle. The most important aspects of a successful oral **contraceptive** product are effective **contraception**, good cycle control (absence of spotting and breakthrough bleeding and occurrence of withdrawal bleeding), and minimal side effects. Combination oral **contraceptives** have traditionally acted by suppression of gonadotropins. In addition, it appears that the progestin component is primarily responsible for **contraceptive** efficacy through inhibition of ovulation, and other peripheral effects which include changes in the cervical mucus (which increase the difficulty. . .
SUMM Since the introduction of oral **contraceptives** (OCs) over a quarter-century ago, research has been directed toward developing preparations that minimize the potential for side effects while. . .
SUMM . . . of racemic norgestrel. It is strongly progestational, has no inherent estrogenic activity, is antiestrogenic, and possesses good biologic activity. The **contraceptive** effects of levonorgestrel are manifested throughout the hypothalamic- pituitary-gonadal-target organ axis.
SUMM In keeping with the goal of reducing the total steroidal dosage, while maintaining **contraceptive** efficacy, good cycle control, and minimizing side effects, numerous regimens have been developed in which the progestin/estrogen combination is administered. . . combination is typically administered for 21 days followed by either a 7-day pill free period or the administration of a non-**contraceptive** placebo (or iron supplement) for 7 days. In these regimens, 3-ketodesogestrel (3-KDSG), desogestrel (DSG), levonorgestrel (LNg), gestodene (GTD), norgestrel (NG),. . .
SUMM Erlich (German Patent DE 4,104,385 Cl and U.S. Pat. No. 5,280,023) discloses sequential **contraceptive** regimens consisting of the administration of an estrogen which effects a disturbance of follicle stimulation, followed by the administration of. . .
SUMM . . . EE) for 4-10 days for a total administration of at least 28 days per cycle. The use of 100-300 .mu.g **drospirenone** and 10-40 .mu.g EE as the 23-24 day progestin/estrogen combination is disclosed. Lachnit also discloses a triphasic plus bridging regimen. .
SUMM Spona (PCT Publication WO 95/17194) discloses **contraceptive** regimens which consist of the administration of a combinaton of a progestin (50-75 .mu.g GTD, 75-125 .mu.g LNg, 60-150 .mu.g. . .
SUMM . . . equivalent to 20 .mu.g EE. It is preferred that the three phases be 8 days each. Following the 24 day **contraceptive** steroid administration, a placebo may be administered for 4 days, the 4 day interval may be pill free, or a. . .
SUMM . . . day phase, a second 6-8 day phase, and a third 6-8 day phase, with it being preferred that the three **contraceptive** steroid

phases be 7 days each. Bennick discloses that the first **contraceptive** steroid phase consists of a progestin at a daily dosage equivalent to 75-150 .mu.g DSG and an estrogen at a daily dosage equivalent to 20-25 .mu.g EE; the second **contraceptive** steroid phase consists of a progestin at a daily dosage equivalent to 75-125 .mu.g DSG and an estrogen at a daily dosage equivalent to 20 .mu.g EE; and the third **contraceptive** steroid phase consists of a progestin at a daily dosage equivalent to 75-100 .mu.g DSG and an estrogen at a daily dosage equivalent to 20 .mu.g EE. Placebo is administered for 7 days following the 21-day **contraceptive** steroid period. Bennick discloses that the progestin may be 3-KDSG, DSG, LNg, or GTD.

SUMM . . . 4,962,098) discloses triphasic progestin/estrogen combinations in which the amount of the estrogenic component is increased stepwise over the three phases. **Contraceptive** steroid combinations are taken for 4-7 days during the first phase (5 days being preferred); for 5-8 days during the. . . preferred); and for 7-12 days during the third phase (9 days being preferred). Following the administration of 21-days of the **contraceptive** steroid combination, placebo is taken for 7 days. For all three phases, 0.5-1.5 mg of norethindrone acetate is used in. . .

SUMM Pasquale (U.S. Pat. No. 4,628,051) discloses triphasic progestin/estrogen combination regimens in which **contraceptive** steroid is administered for 21 days. **Contraceptive** steroid combinations are taken for 5-8 days during the first phase (7 days being preferred); for 7-11 days during the. . .

SUMM . . . .mu.g EE is administered for 9-11 days in the third phase. Placebo is administered for 7 days following the 21-day **contraceptive** steroid regimen.

SUMM . . . combination regimens in which a dose of 20-50 .mu.g EE is administered in all three phases in combination with a **contraceptively** effective daily dose of progestin in the first phase, 1.5-2 times that dose of progestin in the second phase, and. . .

SUMM . . . preferred that each of the three phases is 7 days. Placebo is administered for 6-8 days following administration of the **contraceptive** steroid combination. A specific regimen discloses a first phase of 7 days of 0.5 mg NE in combination with 35. . .

SUMM Upton (EP Patent Specification 253,607 B1) teaches the use of low dose progestin/estrogen combinations for combined hormone replacement therapy and **contraception** in climacteric women. Climacteric women are defined in Upton as pre- menopausal women around 40 years of age whose hormone. . .

SUMM Sartoretto (Clinica e Terapeutica 3: 399 (1974)) discloses a monophasic **contraceptive** regimen consisting of the administration of a combination 100 .mu.g LNg and 20 .mu.g EE for 21 days.

SUMM Pasquale (U.S. Pat. No. 4,921,843) discloses combination progestin/estrogen **contraceptive** regimens which contain 0.5 to 1 mg of progestin and an estrogen having a dose equivalent to 10-40 .mu.g of. . .

SUMM . . . are administered for 10-12 days in the second phase. Placebo is administered for 5-7 days following the administration of the **contraceptive** steroid regimen.

SUMM Oettel (EP 628,312 A1) discloses combination **contraceptive** combinations containing the combination of three components: a biogenic estrogen (estradiol, estrone, or estriol), a synthetic estrogen (EE or mestranol),. . .

SUMM Oettel (EP 696,454 A2) discloses a three phase **contraceptive** regimen in which the first phase consists of the administration for 3-4 days of a composition containing at least one. . .

DETD This invention provides a bridged triphasic combination progestin/estrogen oral **contraceptive** regimen for females of

child-bearing age that provides effective **contraception**, good cycle control, and minimal side effects while greatly reducing the total **contraceptive** steroid administered (particularly the estrogenic component) per 28-day cycle. To achieve the substantial reduction in the total **contraceptive** steroid administered per cycle, the low dose progestin/estrogen combination is administered for 23-25-days per cycle according to a triphasic regimen that is described below. Administration of the **contraceptive** progestin/estrogen combination is begun on the first day of menses (day 1), and continued for 23-25 consecutive days. Following the. . .

DETD More particularly, this invention provides a method of **contraception** which comprises administering to a female of child bearing age a first phase of a combination of a progestin at. . .

DETD The following daily dosages of a combination of levonorgestrel and ethinyl estradiol are preferred for **contraception** when administered according to a bridged triphasic rising regimen for 23-25 consecutive days beginning on the first day of menses,. . .

DETD The following daily dosages of a combination of levonorgestrel and ethinyl estradiol are preferred for **contraception** when administered according to a triphasic mid- peak regimen for 23-25 consecutive days beginning on the first day of menses,. . .

DETD It is preferred that the combination progestin/estrogen **contraceptive** be administered in unit dosage form i.e., tablet or pill, with each unit providing the entire daily dosage. It is. . . be prepared by conventional methodology that is well known to one skilled in the art. In each dosage unit, the **contraceptively** active progestin and estrogen are combined with excipients, vehicles, pharmaceutically acceptable carriers, and colorants. For example, the following illustrates an acceptable composition of a **contraceptive** progestin/estrogen combination of this invention.

DETD This invention also provides a **contraceptive** kit adapted for daily oral administration which comprises, 3-8 first phase dosage units each containing fixed dosage of a combination. . .

CLM What is claimed is:

1. A method of **contraception** which comprises administering to a female of child bearing age for 28 consecutive days, a first phase combination of a. . .

22. A **contraceptive** kit adapted for daily oral administration which comprises; 3-8 first phase dosage units each containing a combination of a progestin. . .

23. The **contraceptive** kit according to claim 22 wherein the progestin is the same for all phases and is selected from the group. . .

24. The **contraceptive** kit according to claim 23, wherein the total number of first phase plus second phase plus third phase dosage units. . .

25. The **contraceptive** kit according to claim 24, wherein the number of first phase dosage units equals 7, the number of second phase.

. . .

26. The **contraceptive** kit according to claim 24, wherein the number of first phase dosage units equals 5, the number of second phase.

. . .

IT 50-28-2, 17.beta.-Estradiol, biological studies 51-98-9, Norethisterone acetate 53-16-7, Estrone, biological studies **57-63-6**, Ethinyl estradiol 57-83-0, Progestin, biological studies 68-22-4, Norethindrone 72-33-3, Mestranol. 797-63-7, Levonorgestrel 6533-00-2, Norgestrel 35189-28-7, Norgestimate. 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene
(triphasic combination of progestin/estrogen female oral contraceptives)

L9 ANSWER 22 OF 23 USPATFULL

AB This invention relates to a method of inducing **contraception** comprising administering an estrogen selected from

2.0 to 6.0 mg of 17.beta.-estradiol and

0.015 to 0.020 mg of **ethinylestradiol;**

and a gestagen selected from

0.05 to 0.075 mg of gestodene,

0.075 to 0.125 mg of levonorgestrel,

0.06 to 0.15 mg of desogestrel,

0.06 to 0.15 mg of 3-ketodesogestrel,

0.1 to 0.3 mg of **drospirenone,**

0.1 to 0.2 mg of cyproterone acetate,

0.2 to 0.3 mg of norgestimate and

>0.35 to 0.75 mg of norethisterone

for a female of reproductive age, who has not yet reached premenopause, by administration for 23 or 24 days, beginning on day one of the menstrual cycle, followed by 5 or 4 pill-free or sugar pill days, during a total of 28 days in the administration cycle.

AN 96:113924 USPATFULL

TI Composition for **contraception**

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D usterberg, Bernd, Spirdingseestrasse 27, D-12307 Berlin, Germany, Federal Republic of
L udicke, Frank, c/o Hopital Cantonal Universitaire, 32bis, Bld de la Cluse, CH-1211 Geneva 4, Switzerland <--

PI US 5583129 19961210
AI US 1994-268996 19940630 (8)
PRAI DE 1993-4344462 19931222
DT Utility
FS Granted
EXNAM Primary Examiner: Spivack, Phyllis G.
LREP Millen, White, Zelano, & Branigan, P.C.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 356
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Composition for **contraception** <--
PI US 5583129 19961210
AB This invention relates to a method of inducing **contraception** comprising administering an estrogen selected from
AB 0.015 to 0.020 mg of **ethinylestradiol;**
AB 0.1 to 0.3 mg of **drospirenone,**
SUMM This invention relates to the common use of estrogens and gestagens for the production of a combination preparation for oral **contraception** and a corresponding pack containing this combination preparation.
SUMM Combination preparations for oral **contraception** are already known, for example, Femovan.RTM. [DE-PS 2 546 062] or Marvelon.RTM. [DE-OS 2 361 120]. These preparations consist of. . . placebos). The dose to be administered daily is uniformly high in each case (so-called single-phase preparations) and produces the desired **contraceptive** effect in the entire intake period and in the

intake pause or during the intake of the placebos. In most. . .

SUMM . . . Pasquale) or completely (Kuhl) bridged over by estrogen-containing dosage units. In this case, it is possible that the synthetic estrogen **ethinylestradiol** otherwise contained in oral **contraceptives** is replaced partially or completely by a conjugated estrogen, preferably estradiol.

SUMM A combination preparation for substitution therapy and **contraception** for females before menopause (approximately starting from the 40th year of life) is known from EP-A-0 253 607. This combination. . .

SUMM **ethinylestradiol** and

SUMM . . . by the hormonal changeover of the female organism in this phase. Such a composition simultaneously assures a premenopausal female the **contraceptive** protection still necessary at this age.

SUMM The development of new oral **contraceptives** for females of reproductive age before premenopause was characterized during the last twenty years above all by the reduction of. . .

SUMM . . . the meantime confirm the desired trend toward better compatibility of lower-dosed preparations relative to cardiovascular complications [(1.) Thorogood, M., Oral **Contraceptives** and Cardiovascular Disease: An Epidemiologic Overview; Pharmacoepidemiology and Drug Safety, Vol. 2: 3-16 (1993); (2.) Gerstman, B. B.; Piper, J. M.; Tomita, D. K.; Ferguson, W. J.; Stadel, B. V.; Lundin, F. E.; Oral **Contraceptive** Estrogen Dose and the Risk of Deep Venous Thromboembolic Disease, Am. J. E., Vol. 133, No. 1, 32-36 (1991); (3.) Lidegaard, O., Oral **contraception** and risk of a cerebral thromboembolic attack: results of a case-control study; BMJ Vol. 306, 956-63 (1993); (4.) Vessey, M.; Mant, D.; Smith, A.; Yeates, D.; Oral **contraceptives** and venous thromboembolism: findings in a large prospective study; BMJ, Vol. 292, (1986); (5.) Mishell, D. R., Oral **Contraception**: Past, Present and Future Perspectives; Int. J. Fertil., 36 Suppl., 7-18 (1991)].

SUMM . . . above all between the level of the estrogen dose and the incidence of cardiovascular diseases. But the maintenance of the **contraceptive** effectiveness stands in the way of an extreme reduction of the daily estrogen dose. Although the ovulation-inhibiting effect of the low-dosed oral **contraceptives** is caused mainly by the gestagenic component, the estrogenic component also makes a significant contribution to the central inhibition action. . .

SUMM The lowest estrogen dose contained in an oral **contraceptive** on the market at this time is 20 .mu.g of **ethinylestradiol**, combined with 150 .mu.g of desogestrel (Mercilon). Although the cycle control of this preparation is, as expected, somewhat poorer in. . . But the observation, made identically in several studies, of a lesser ovarial suppression of the preparation containing 20 .mu.g of **ethinylestradiol** represents a clinically important problem. Obviously with this very low estrogen dose, in the case of many females, the maturation. . . studies or hormonal studies, results [(6.) Lunell, N. O.; Carlstr om, K.; Zador, G.; Ovulation inhibition with a combined oral **contraceptive** containing 20 .mu.g of **ethinylestradiol** and 250 .mu.g of levonorgestrel; Acta. Obstet. Gynecol. Scand. Suppl. 88: 17-21 (1979); (7.) Mall-Haefeli, M.; Werner-Zodrow, I.; Huber, P.. . . and Gynecology] 51, 35-38, Georg Thieme Verlag, Stuttgart-New York (1991); (8.) Strobel, E., Behandlung mit oralen Kontrazeptiva [Treatment with Oral **Contraceptives**]; Fortschr. Med. Vol. 110, No. 20 (1992); (9.) Letter to Editor, **Contraception** 45: 519-521 (1992); (10.) Teichmann, A. T.; Brill, K.; Can Dose Reduction of **Ethinylestradiol** in OCs Jeopardize Ovarian Suppression and Cycle Control? Abstract Book, VIIIth World Congress on Human Reproduction, Bali, Indonesia (1993)].

SUMM . . . The requirements for an ovulation would thus be present. It is estimated that approximately one third of females take oral **contraceptives** irregularly within one year of use (Gynpress, Volume 1, No. 3, 1990). The risk of a pregnancy is therefore high especially in the case of intake errors with the 20 .mu.g

ethinylestradiol preparations.

DETD 0.015 to 0.020 mg of **ethinylestradiol**;

DETD 0.1 to 0.3 mg of **drospirenone**,

DETD for the production of a form of dosage for **contraception** for a female of reproductive age, who has not yet reached premenopause, by administration of the form of dosage for. . .

DETD 0.020 mg of **ethinylestradiol**;

DETD 0.25 to 0.30 mg of **drospirenone**,

DETD for the production of a form of dosage for **contraception** as described above.

DETD In addition, this invention relates to a combination product for oral **contraception**, which comprises

DETD 0.020 mg of **ethinylestradiol**;

DETD 0.25 to 0.30 mg of **drospirenone**,

DETD An especially preferred combination preparation according to this invention comprises 23 dosage units, each containing 20 .mu.g of **ethinylestradiol** and 75 .mu.g of gestodene and 5 sugar pills or other indications to show that no dosage unit or a. . .

DETD The clinical study briefly described below was performed with **ethinylestradiol** as estrogen and gestodene as representative of the substance class of the gestagens possible according to the invention. All possible combinations of **ethinylestradiol** or estradiol according to the invention in the indicated dosages with one of the selected gestagens in the indicated dosages. . .

DETD The 23-day administration of 20 .mu.g of **ethinylestradiol** in combination with 75 .mu.g of gestodene results, in comparison to the 21-day administration, in a stronger ovarian suppression. In. . .

DETD . . . according to the invention thus achieves the effectiveness previously known for preparations with a daily content of 30 .mu.g of **ethinylestradiol**, although the daily **ethinylestradiol** dose is 33% lower and also the total dose per cycle is 27% lower.

DETD The advantages of a combination preparation for oral **contraception** to be administered over 23 days relative to the usual 21-day preparations with less than 30 .mu.g of **ethinylestradiol** can be characterized as follows:

DETD . . . the 23-day preparation relative to a maximum of 40% among those who received the 21-day preparation). This means a greater **contraceptive** reliability of the 23-day preparation, especially in the case of previous intake errors. The danger of "breakthrough ovulations" is smaller.

DETD In summary, an intake, extended by two (or three) days, of preparations containing 20 .mu.g of **ethinylestradiol** in each daily dosage unit can produce the above-mentioned advantages, without the daily dose having to be raised to the previously largely used level of 30 .mu.g of **ethinylestradiol**.

DETD . . . for a combination preparation according to the invention takes place completely analogously as it is already known for usual oral **contraceptives** with 21-day intake period of the active ingredients, such as, for example, Femovan.RTM. (**ethinylestradiol**/gestodene) or Microgynon.RTM. (**ethinylestradiol**/levonorgestrel).

DETD A pack containing a combination preparation according to the invention is also designed analogously to packs for already known oral **contraceptives** on the market with the variation that instead of the usual 21 dosage units containing the active components, now 23. . .

DETD . . . the statements made in EP-A 0 253 607, especially also to the statements there for determination of equivalent amounts of **ethinylestradiol** and 17.beta.-estradiol, on the one hand, and various gestagens, such as levonorgestrel, desogestrel, 3-ketodesogestrel and gestodene, on the other hand.

DETD . . . Agent Research) 27, 2a, 296-318 (1977), as well as to "Aktuelle Entwicklungen in der hormonalen Kontrazeption" [Current Developments in Hormonal **Contraception**]; H. Kuhl in Gyn akologe"

[Gynecologist] 25: 231-240 (1992).

DETD FIG. 1: Area with the 17.beta.-estradiol level in groups of 30 females, who are treated with an oral **contraceptive** (75 .mu.g of gestodene +20 .mu.g of **ethinylestradiol**) in 21- or 23-day administration interval over three cycles.

DETD . . . Number of females in %, who showed follicular developments (>13 mm diameter) with 21- or 23-day treatment with an oral **contraceptive** (75 .mu.g of gestodene +20 .mu.g of **ethinylestradiol**).

CLM What is claimed is:

1. A method of inducing **contraception** in a female of reproductive age who has not yet reached premenopause, comprising administering to said female a composition comprising an estrogen selected from 2.0 to 6.0 mg of 17.beta.-estradiol and 0.015 to 0.020 mg of **ethinylestradiol**; and a gestagen selected from 0.05 to 0.075 mg of gestodene, 0.075 to 0.125 mg of levonorgestrel, 0.06 to 0.15 mg of desogestrel, 0.06 to 0.15 mg of 3-ketodesogestrel, 0.1 to 0.3 mg of **drospirenone**, 0.1 to 0.2 mg of cyproterone acetate, 0.2 to 0.3 mg of norgestimate and >0.35 to 0.75 mg of norethisterone;. . .

2. A method according to claim 1, whereby the estrogen is **ethinylestradiol**.

6. A method according to claim 1, whereby the gestagen is cyproterone acetate or **drospirenone**.

7. A method according to claim 1, whereby the composition comprises an estrogen selected from >2.0 to 6.0 mg of 17.beta.-estradiol and 0.020 mg of **ethinylestradiol**; and a gestagen selected from >0.06 to 0.075 mg of gestodene, >0.100 to 0.125 mg of levonorgestrel, >0.10 to 0.15 mg of desogestrel, >0.10 to 0.15 mg of 3-ketodesogestrel, 0.25 to 0.30 mg of **drospirenone**, 0.1 to 0.2 mg of cyproterone acetate, 0.2 to 0.3 mg of norgestimate and 0.50 to 0.75 mg of norethisterone.

. . .

8. A method according to claim 1, whereby the estrogen is present in a dose of 20 .mu.g of **ethinylestradiol** or an equivalent dose of 17.beta.-estradiol and the gestagen is present in a dose of 75 .mu.g of gestodene or an equivalent dose of levonorgestrel, cyproterone acetate or **drospirenone**.

IT 50-28-2, Estradiol, biological studies **57-63-6**, Ethynylestradiol 68-22-4, Norethisterone 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene **67392-87-4**, Drospirenone
(low-dose contraceptive compn. contg. estrogen and gestagen)

L9 ANSWER 23 OF 23 USPATFULL

AB Dihydrospirorenone, ##STR1## preferably together with an estrogen, can be used for the production of a pharmaceutical agent suitable for treatment of hormonal irregularities during premenopause (menstruation stabilization), for hormonal substitution therapy during menopause, for treatment of androgen-induced disorders and/or for **contraception**.

AN 96:99204 USPATFULL

TI Dihydrospirorenone as an antiandrogen

IN Beier, Sybille, Berlin, Germany, Federal Republic of
Elger, Walter, Berlin, Germany, Federal Republic of
Nishino, Yukishige, Berlin, Germany, Federal Republic of
Wiechert, Rudolf, Berlin, Germany, Federal Republic of

PA Schering Aktiengesellschaft, Berlin, Germany, Federal Republic of (non-U.S. corporation)

PI US 5569652 19961029 <--

AI US 1993-162387 19931207 (8)

RLI Continuation of Ser. No. US 1992-835000, filed on 14 Feb 1992, now abandoned which is a continuation of Ser. No. US 1990-524396, filed on 16 May 1990
PRAI DE 1989-3916112 19890516
DT Utility
FS Granted
EXNAM Primary Examiner: Criares, Theodore J.
LREP Millen, White, Zelano, & Branigan, P.C.
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 270
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5569652 19961029 <--
AB . . . of hormonal irregularities during premenopause (menstruation stabilization), for hormonal substitution therapy during menopause, for treatment of androgen-induced disorders and/or for **contraception** .
SUMM . . . appears, also exhibits a marked gestagen effect. Therefore, compound I can be used alone or in combination with estrogens in **contraceptive** preparations.
SUMM According to DE-A 30 22 337, these preparations are to be used for women who desire **contraception** and suffer from high blood pressure or in whom blood pressure rises when they take oral **contraceptives**. Thus, also for women predisposed to increased blood pressure, hormonal **contraception** is possible.
SUMM A combined preparation for substitution therapy and **contraception** for women before menopause (starting at about age 40) is known from EP-A 0253 607. This combined preparation contains an. . .
SUMM . . . the discomfort caused by the hormonal change of the female organism during this phase. Simultaneously, such a composition guarantees the **contraceptive** protection still necessary at this age.
SUMM . . . reasons and because of the increase in the incidence of contraindications with increasing age, the taking of the usual hormonal **contraceptives** is recommended for women only until about age 35, so that a hormonal treatment during premenopause and a substitution therapy during menopause using doses that simultaneously have a **contraceptive** effect can be considered problematic.
SUMM . . . strong antiandrogenic activity component, and specifically at doses that also make possible the formulation of this compound as an oral **contraceptive**. Dihydrospirorenone acts as an antiandrogen about as strongly as cyproterone acetate, considered the standard compound (same maximum effect). (Animal model:. . .
SUMM . . . during premenopause (e.g., menstruation stabilization) and/or for hormonal substitution therapy during menopause and/or for treatment of androgen-induced disorders and/or for **contraception**. Conventional protocols can be used to determine antiandrogenic activity, e.g., as disclosed in Methods in Hormone Research, Editor: R. I.. . . .
SUMM . . . a method of treating an androgen induced disorder in a female comprising administering I; to a method of achieving a **contraceptive** effect in a female during premenopause or menopause (both terms having their conventional meaning, e.g., as shown in "The Controversial. . .
SUMM . . . with the compound of formula I. Whether a synthetic or a natural estrogen is preferably used depends on whether the **contraceptive** effect or the substitutive effect is emphasized: in the first case, ethynylestradiol or another synthetic estrogen is preferred, in the. . .
SUMM . . . a pharmaceutical agent guarantees a woman of middle age (about age 35-55) a stabilization of her menstruation cycle and the **contraception** still indispensable at this age, with simultaneous, favorable influence on androgen-induced disorders. Of

course, this pharmaceutical agent is also suited. . .

CLM What is claimed is:
11. A method of simultaneously achieving, during premenopause or menopause, a **contraceptive** effect, an anti-androgenic effect, and an anti-aldosterone effect in a female patient in need thereof comprising administering an effective amount. . .

IT **67392-87-4**, Dihydrospirorenone
(antiandrogen, for treatment of hormonal disturbances)

IT **57-63-6**, 17.alpha.-Ethinylestradiol
(hormonal disturbances treatment by dihydrospirorenone and)